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A Method for Indirect Pulse Recording, and Its Use in the Diagnosis of Aortic Stenosis

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Although the clinical diagnosis of aortic stenosis usually is possible after careful evaluation of the patient's history, physical findings, chest x-ray, and electrocardiogram, a satisfactory objective measure of the presence and degree of aortic valvular stenosis would be of value. In this paper I shall review measures now in use and introduce a method for indirect recording of the pulse by means of an electronic pneumoplethysmograph which appears to offer a number of advantages.

OTHER METHODS REVIEWED

Miller and White[1] reviewed both the mechanical and optical[2] systems of pulse recording and proposed the recording of the pulse wave by an electrical system which utilized a crystal microphone as a pickup. By 1947, according to Grishman, Steinberg, and Sussman,[3] configuration of pulse tracings over the innominate and carotid arteries had won recognition as the most important single diagnostic sign of aortic stenosis.

The necessary peripheral artery pressure curves were obtained in a number of ways: Brofman and Feil[4] used optical registration along with the Frank segment capsule. Reinhold and associates[5] recorded arterial tracings by placing a metal stylus on the suprasternal notch overlying the carotid artery (the impulses were transmitted directly to a crystal of Rochelle salt and the voltage amplified and fed into a mirror galvanometer). Donoso, Sapin, Kuhn and Grishman[6] placed a crystal microphone over the carotid arteries. Goldberg, Bakst, and Bailey[7] employed direct brachial artery puncture. Hancock and Abelmann,[8] who also used brachial artery puncture in their 250 patients, came to the conclusion that "brachial artery pulse contour may serve to confirm a clinical diagnosis of aortic stenosis but is not diagnostic of aortic stenosis, and in any individual patient yields no information as to the severity of the lesion."

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METHOD

A new, versatile, and highly sensitive electronic pneumoplethysmograph[9] was used in this study. This instrument records accurately the pulse volume of a limb segment by recording volume changes of the part (in cubic centimeters). The pulse wave may be amplified by increasing the sensitivity of the instrument, and the tracing may be standardized easily. The unit is lightweight, portable, and easy to use.

The plethysmograph was attached to a modified blood pressure cuff applied just above the elbow on the right arm; the brachial artery puncture was usually performed on the left side. The brachial artery pulse curve was recorded (via a strain gauge) simultaneously with the plethysmographic pulse curve on a Sanborn Twin-Beam Electrocardiograph. In instances in which the records were not taken simultaneously, they were recorded either on the Sanborn Twin-Beam Electrocardiograph or on the Sanborn Viso-Cardiette.

Plethysmograms were taken with the cuff inflated to systolic blood pressure level, and additional records were taken as the pressure in the cuff was lowered in 10-mm. decrements. Usually, the largest and most accurate pulse waves were recorded at or about diastolic blood pressure level; it was from these curves that all measurements were made.

On each tracing, measurements were made of the duration of systolic ejection, i.e., the time interval from the onset of the wave to its peak or apex. This time interval has been variously called the "onset-to-peak time," the "crest time," or simply "the duration of the upstroke."

TABLE I. CORRELATION OF PLETHYSMOGRAM AND BRACHIAL ARTERY CURVE IN 25 PATIENTS

PATIENT		CREST TIME (SEC.)		CORRELATION	SIMULTANEOUS CURVE	DIAGNOSIS
		BRACHIAL ARTERY	PLETHYSMOGRAM			
1.	A.E.	0.26	0.28	Excellent	No	A.S. and A.I. clinically
2.	J.B.	0.08	0.08–0.12	Good	No	Normal heart
3.	C.A.	0.20–0.22	0.20–0.22	Excellent	No	A.S. proved at surgery
4.	M.B.	0.12	0.12	Excellent	No	Interatrial septal defect
5.	V.R.	0.11*	0.21	Poor*	Yes	A.S., A.I., M.S., M.I. clinically
6.	G.P.	0.26	0.27	Excellent	Yes	A.S. proved at surgery
7.	E.G.	0.20	0.20	Excellent	Yes	A.S. clinically
8.	L.S.	0.24	0.26	Excellent	Yes	A.S. proved at surgery
9.	D.M.	0.16	0.16	Excellent	Yes	No valvular disease
10.	H.H.	—	0.24–0.26	—	No	A.S. proved at surgery
11.	H.D.	0.12–0.16	0.16	Good	Yes	M.S., (?) A.S. clinically
12.	N.F.	0.20	0.20	Excellent	Yes	M.S., A.S. proved at surgery
13.	J.R.	—	0.24	—	No	M.S., A.S. proved at surgery
14.	D.G.	0.24	0.24	Excellent	No	A.S. proved at surgery
15.	D.R.	0.15–0.16	0.14–0.15	Excellent	Yes	M.I. clinically
16.	M.G.	0.08*	0.22–0.24	Poor*	Yes	Loud systolic murmur 3rd left intercostal space; normal cardiac catheterization
17.	H.O.	0.22–0.24	0.22–0.24	Excellent	Yes	M.S., A.S. clinically
18.	T.K.	0.14–0.16	Poor curve	—	Yes	A.S., A.I. clinically
19.	A.C.	0.11–0.16	0.11–0.16	Excellent	Yes	M.S. (mild) clinically
20.	R.M.	0.12–0.24*	0.24	Poor*	No	A.S. proved at surgery
21.	R.H.	0.16	0.16	Excellent	Yes	A.S.H.D. proved at surgery (no valvular disease)
22.	L.P.	0.24	0.24	Excellent	No	A.S. clinically
23.	D.L.	0.20	0.20	Excellent	Yes	M.S. clinically
24.	J.H.	0.16	0.16	Excellent	Yes	M.S., M.I., (?) A.S. clinically
25.	J.S.	0.12–0.20*	0.20	Poor*	No	A.S. clinically

*See text for explanation.
M.S. = mitral stenosis; M.I. = mitral insufficiency; A.S. = aortic stenosis; A.I. = aortic insufficiency.

These measurements are usually accurate in the range of 0.01 to 0.02 second, although the measurements may be less accurate if the apex of the wave is rounded or flattened. Correlation between plethysmographic and brachial artery pressure curves was considered "excellent" if the difference in timing was 0.02 second or less, "good" if the difference was between 0.02 and 0.04 second, and "poor" if the difference was over 0.04 second.

Segmental plethysmograms were obtained on 25 patients: 15 of the plethysmograms were recorded simultaneously with the brachial artery pressure curves; 8 were recorded separately; and 2 were recorded in patients with the clinical diagnosis of aortic stenosis on whom a brachial artery puncture had not been performed.

RESULTS

The results are shown in Table I. The correlation between the plethysmographic and the brachial artery pressure curves was "excellent" in 16 patients, "good" in 2 patients, and "poor" in 4 patients (possible explanations for the "poor" results will be discussed below). In 2 additional patients only the plethysmogram was taken. In 1 patient the plethysmogram was too poor to interpret.

DISCUSSION

Because of the recent improvement in surgical techniques, aortic commissurotomy is now an accepted therapeutic procedure in selected patients with aortic stenosis. The brachial artery pulse curve is now in use in many cardiac clinics to confirm the presence, and estimate the degree, of aortic stenosis, aid in the selection of candidates for aortic commissurotomy, and evaluate results of that surgical procedure. However, a technique for obtaining an accurate indirect peripheral pulse wave would be useful for the reasons that the brachial artery puncture (1) is moderately expensive and physically uncomfortable for the patient; (2) requires complex equipment and the services of at least one physician plus a nurse or technician; and (3) is time-consuming in its preparation and often in performance. In contrast to brachial artery puncture, plethysmography may be performed rapidly, inexpensively, and without trauma, by relatively unskilled personnel.

A close correlation was obtained between the plethysmograms and the brachial artery curves, except in four cases. These are sufficiently important to be discussed individually: In Patients 5 and 16 (see Fig. 1) a plateau is present on the catacrotic limb of the brachial artery curve, between the peak of the curve and the dicrotic notch. The peak of the plethysmographic curve is identical in timing with this plateau. Patient 5 had clinical signs and symptoms of multivalvular disease, including involvement of the aortic valve; a loud systolic murmur was heard at the third left intercostal space in Patient 16, who proved upon cardiac catheterization to have a "hemodynamically normal" heart. The pulse waves in Patients 20 and 25 (see Figs. 2 and 3) illustrate that the plateau or notch in the catacrotic limb of the brachial artery curve may occasionally become the peak of the wave, while the peak of the plethysmogram consistently is concurrent in time with the plateau of the arterial curve. Subaortic stenosis with a marked pressure gradient between the left ventricle and the aorta was proved at surgery in Patient 20; in Patient 25 the clinical diagnosis was aortic stenosis. In summary,

the plethysmographic curves from these four patients would seem to indicate that all four had aortic stenosis by virtue of the prolonged crest time in each case, but the brachial artery curves revealed only intermittent prolongations of the crest times in two of them and normal crest times in the other two. Of these four patients, one had proven aortic stenosis, two had clinical diagnoses of aortic stenosis, and one had a loud systolic murmur with normal findings on cardiac catheterization. In these patients the plethysmogram was as reliable, if not more reliable, than the brachial artery pulse curve.

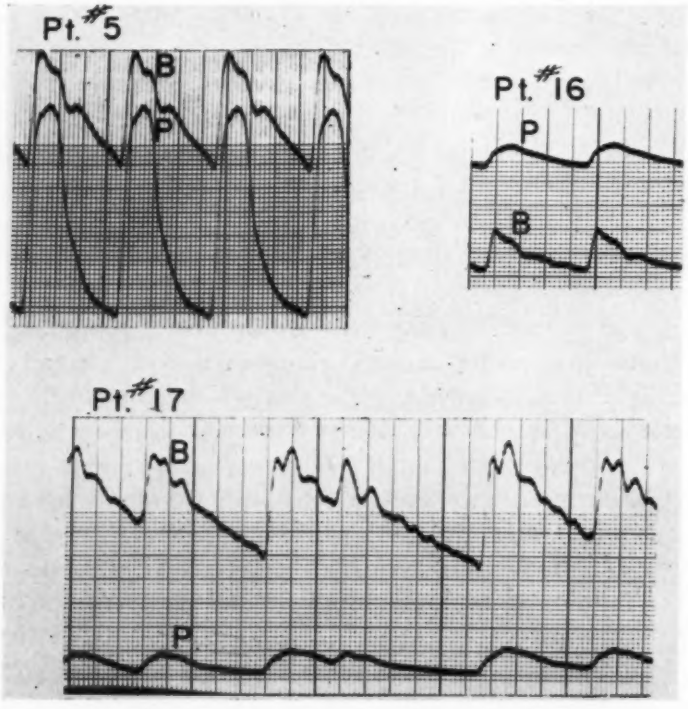

Fig. 1.—*B* is the brachial artery pressure curve, and *P* is the plethysmogram. In Patients 5 and 16 note the plateau or notch on the catacrotic limb of the brachial artery curve which is identical in timing with the peak of the plethysmogram (see text). In Patient 17 the brachial artery curve and the plethysmogram are identical regardless of the contour of the curve.

The plethysmogram seems to be as dependable as the brachial artery curve in all patients; possibly, it may be more accurate in the occasional patient. One possible explanation is that the plethysmogram measures the volume change in a fairly large segment of the extremity, whereas the brachial artery pulse curve is obtained through a relatively small intra-arterial needle which, because of its size, is more prone to magnify any artefact. It is important, of course, that the needle orifice must be neither persistently nor intermittently occluded by the vessel wall. Another possible explanation is that, in contrast to the method of obtaining a plethysmogram, which is always a benign procedure, the trauma involved in a brachial artery puncture may produce in some patients reflex neurovascular changes or a varying cardiac stroke volume which may be reflected in an inaccurate brachial artery curve.

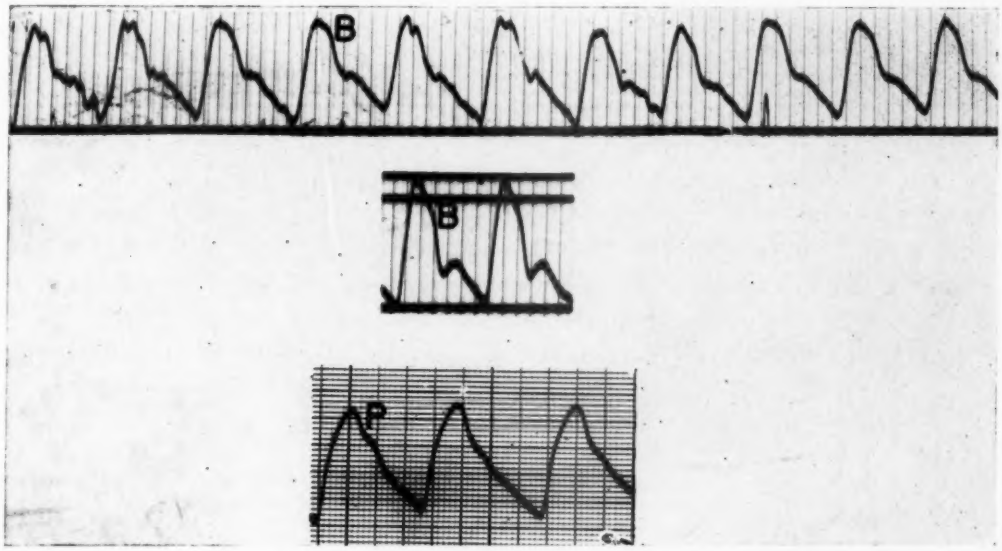

Fig. 2.—Patient 20. The upper two tracings are brachial artery pressure curves (the timing is 0.1 second between the heavy vertical lines), and the lower tracing is a plethysmogram (0.2 second between the heavy vertical lines). Note the variability of the brachial artery curves which show a crest time varying between 0.12 and 0.23 second. The crest time of the plethysmogram is consistently 0.24 second. This patient was proven to have subaortic stenosis at surgery (see text).

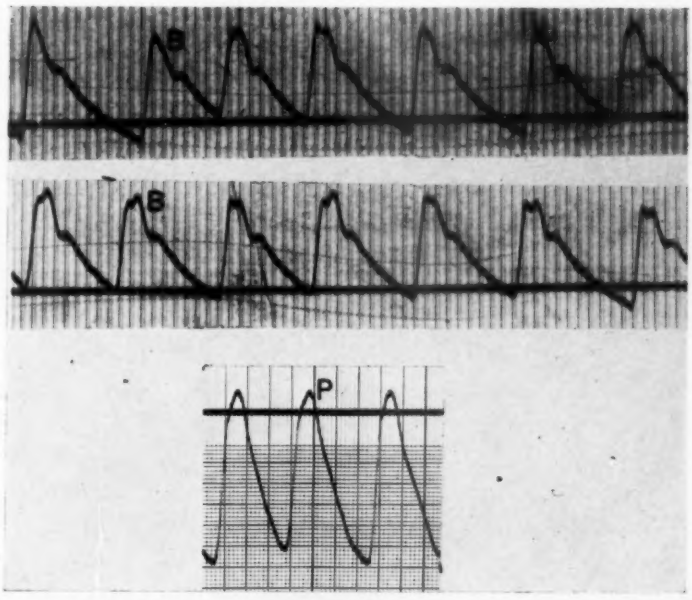

Fig. 3.—Patient 25. The upper two tracings are a continuous brachial artery pressure curve. These curves illustrate the intermittent prolongation of the crest time when the second peak (or the notch on the catacrotic limb) becomes the crest of the wave. The lower tracing is the plethysmogram on the same patient. The heavy vertical lines in the upper tracings represent 0.1 second, and the heavy lines in the lower tracing represent 0.2 second (see text).

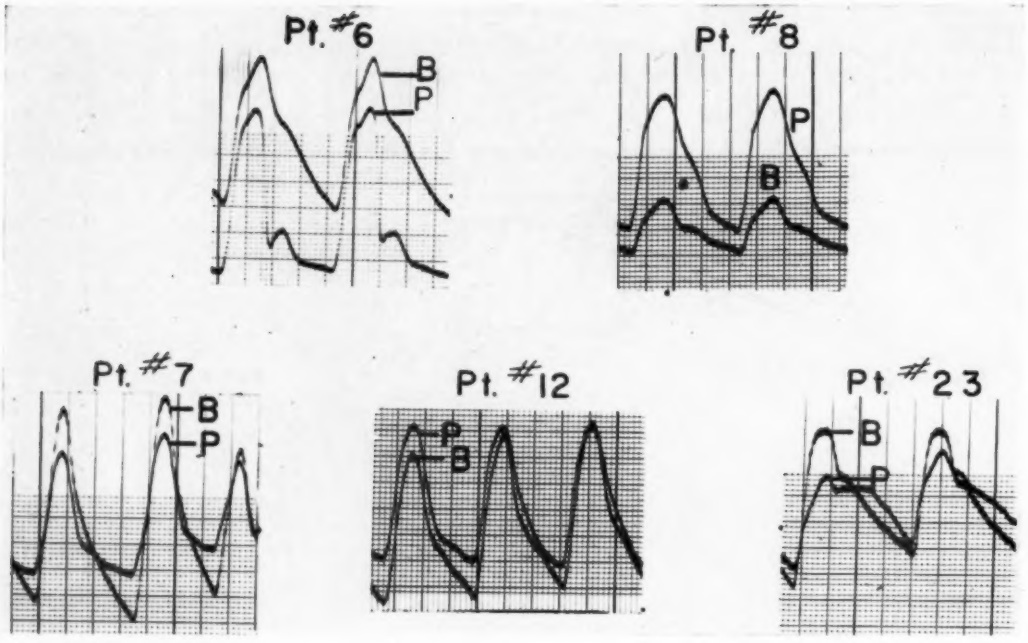

Fig. 4.—*B* is the brachial artery pressure curve, and *P* is the plethysmogram. Patients 6, 8, and 12 had proven aortic stenosis; Patient 7 had the clinical diagnosis of aortic stenosis; and Patient 23 had the clinical diagnosis of pure mitral stenosis.

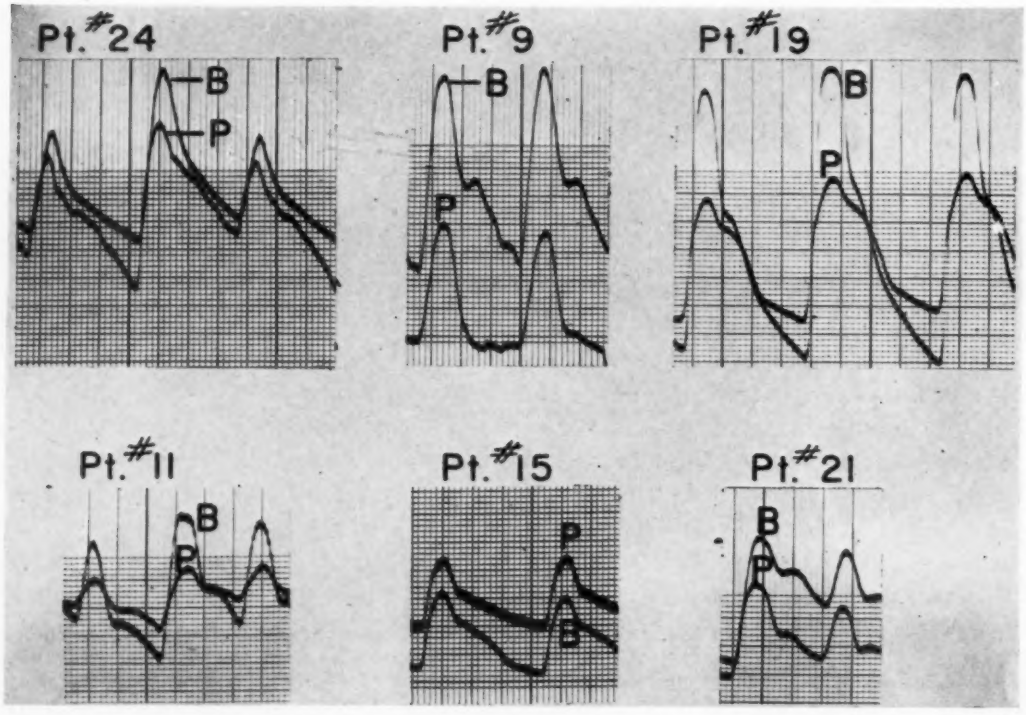

Fig. 5.—Simultaneous curves on patients with a variety of cardiac diagnoses. *B* is the brachial artery pressure curve, and *P* is the plethysmogram.

This preliminary report suggests that the plethysmograph provides a good method for producing an accurate arterial pulse record which is similar to the brachial artery pulse curve, but further comparison is needed before any definite conclusions are drawn.

SUMMARY

A method for obtaining an indirect peripheral pulse curve is described. This method depends on the use of a recently described segmental pneumoplethysmograph. Preliminary results in comparing the plethysmographic curve to the brachial artery pulse curve in patients with and without aortic stenosis are reported. Apparently, in some situations the plethysmogram may be more dependable than the brachial artery curve.

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REFERENCES

1. Miller, A., and White, P. D.: Am. Heart J. **21**:504, 1941.
2. Frank, O.: Ztschr. f. Biol. **50**:341, 1908.
3. Grishman, A., Steinberg, M. F., and Sussman, M. L.: M. Clin. North America **31**:543 1947.
4. Brofman, B. L., and Feil, H.: Circulation **6**:817, 1952.
5. Reinhold, J., Rudhe, U., and Bonham-Carter, R. E.: Brit. Heart J. **17**:327, 1955.
6. Donoso, E., Sapin, S. P., Kuhn, L. A., and Grishman, A.: Pediatrics **18**:205, 1956.
7. Goldberg, H., Bakst, A. A., and Bailey, C. P.: Am. Heart J. **47**:527, 1954.
8. Hancock, E. W., and Abelmann, W. H.: Circulation **16**:572, 1957.
9. Winsor, T.: Angiology **8**:87, 1957.

Difficulties in the Measurement of Pulse-Wave Velocity

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I. INTRODUCTION

The purpose of this paper is to discuss the difficulties encountered in the measurement of pulse-wave velocity. The methods themselves will not be discussed in detail, because they are not pertinent to this paper.

Since the pulse-wave velocity is greater in rigid tubes, a determination of this velocity could be used to give a quantitative estimate as to arterial wall rigidity, either secondary to arteriosclerosis or to age changes.

II. DIFFICULTIES WITH INSTRUMENT REGISTRATION

The accurate measurement of pulse-wave velocity is not a simple matter, as can be demonstrated with the help of an old-fashioned instrument, the Marey tambour. To illustrate, take two tambours and place them so that their pointers rest parallel on a kymograph revolving at a speed of 2.5 cm. per second, in the manner illustrated below. Imagine that the sensing diaphragms are placed on the radial and brachial arteries, respectively, and that the distance between the diaphragms, s, is known. Then the pulse-wave velocity can be computed using the formula

$$v = s/t$$

where s = distance and t = time in seconds (Figs. 1 and 2). However, the actual measurement is not so simple, because, for one thing, the tambour is an instrument of great inherent inertia, and thus cannot follow the more rapid pressure variations. Modern registration methods are also plagued with similar difficulties, which, however, find their origin in the tissues. For further insight, let us take a closer look at the tambour.

1. *Amplitude Characteristics.*—Suppose we strike the tambour. The pointer will vibrate with a resonant frequency (ν_1) that is independent of the applied force, and depends only on the mechanical properties of the tambour, i.e., the length of the pointer arm, et al. Now let us apply artificially a periodic pressure variation of constant amplitude to the tambour, so that it moves in simple harmonic motion, with a given frequency which is small at first, but which is gradually

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increased. We must choose the measured pressure variations small so that the needle excursions are linear with respect to the pressure. Thus, we see the recording of Fig. 3 on the drum as the frequency is increased.

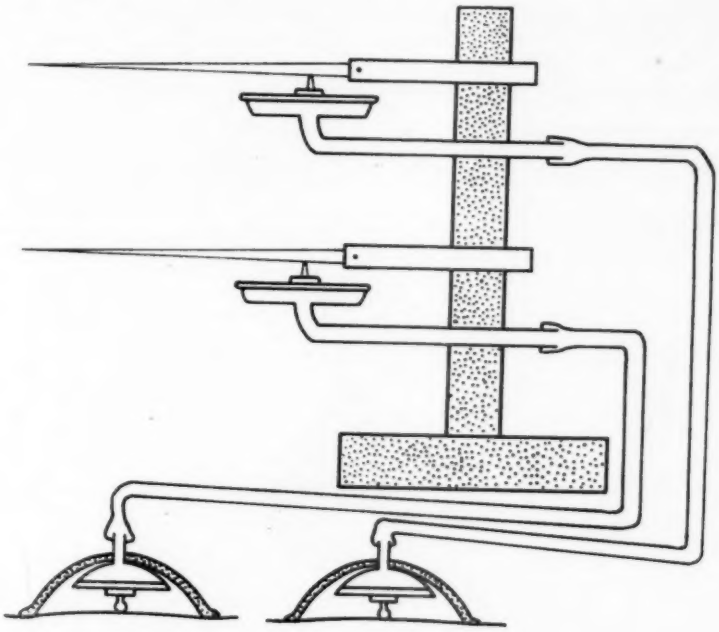

Fig. 1.—Two tambours.

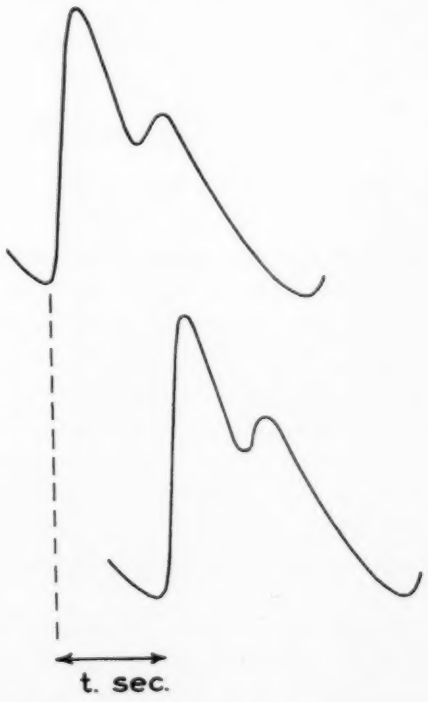

Fig. 2.—Two ideal pulse curves.

At first the needle gives a true recording of the pressure, but as the resonant frequency of the recording system is reached, the excursions become greater in spite of the fact that the pressure variation has remained constant throughout the recording time. Referring again to Fig. 3, we see that if the frequency is further increased, the inertia drag of the tambour becomes excessive and the needle movement ineffective. Therefore, it is apparent that the pressure is correctly recorded only for frequencies appreciably lower than the resonant frequency of the recording system. The height of the maximum in Fig. 3 depends on the damping.

Let us re-examine the pressure curve. A phenomenon which repeats itself with a period $T_2 = \frac{1}{\nu_2}$ (e.g., $T_2 = \pm 1$ sec.) (Fig. 4,*a*) can be considered as the sum of an infinite number of harmonic

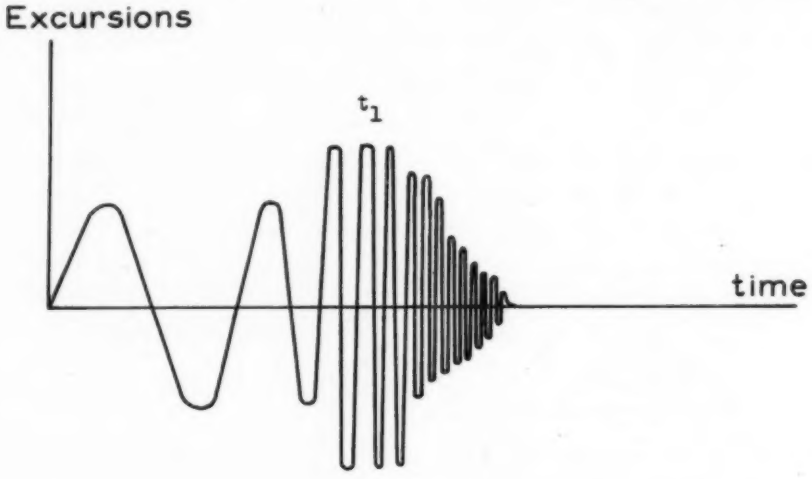

Fig. 3.—Frequency increases with time. At t_1, a frequency ν_1 is passed.

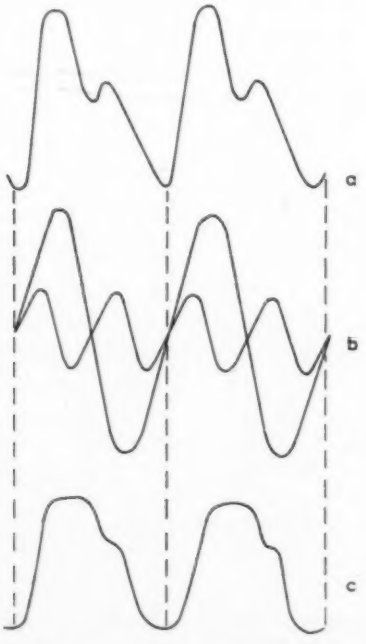

Fig. 4.—*a*, Pulse curve. *b*, Fourier analysis (grand frequency and first harmonic). *c*, Distorted pulse contour.

vibrations with frequencies of ν_2, $2\nu_2$, $3\nu_2$ ad infinitum, each with different amplitude and phase (Fourier analysis, Fig. 4,*b*). In the normal pulse wave, the harmonics which have a frequency greater than 30 cycles per second also have a very low amplitude and are of no practical importance. The tambour magnifies harmonics with a frequency of 3 cycles per second too much if its resonant frequency $\nu_1 = 3$, thereby giving a distorted pressure curve; for example, it gives Fig. 4,*c* instead of Fig. 4,*a*.

Such a distortion can result in a tremendous error in the determination of pulse-wave velocity by simply shifting the foot-point in the distorted curve. It is only by choosing two exactly identical registering systems that this difficulty can be eliminated.

2. *Phase Characteristics.*—It is also true that the tambour will give each harmonic a different shift in the horizontal direction, thereby giving rise to further distortion in the recorded pulse (see Fig. 4).

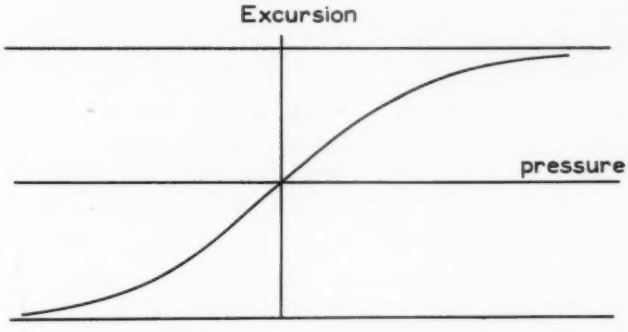

Fig. 5.—The phenomenon of alinearity.

3. *Nonlinearity.*—If amplitude characteristics are to be studied, it is necessary that small pressure variations be chosen, for it is only in the low-pressure range (Fig. 5) that the excursion is proportional to the pressure. Large pressure accretions would be recorded with gross error.

III. EXTRANEOUS TISSUE INTERFERENCE

Difficulties inherent within the recording instrument can be reduced by using more modern instruments which have resonant frequencies greater than 30 cycles per second and adjusted damping. The utilization of such instruments will allow equal magnification of all amplitudes of the different harmonics of the pulse wave, thereby giving a negligible phase shift and also fulfilling the requirements of linearity.

Even with the instrumentation corrected, more difficulties arise. Between the blood, the propagating medium, and the sensing device there are extraneous tissues, namely, the vessel wall and subcutaneous and cutaneous tissues. These tissues function just as a tambour, with all its inherent bad qualities, as discussed above (amplitude distortion, phase shift, and nonlinearity). So, no matter how good our instrument is, the pressure wave will still be registered in a distorted form.

The above-mentioned problem would make little practical difference if the deformation were constant at all registration sites, but tissue characteristics above the lumen of the radial artery differ from, say, tissue characteristics above the brachial artery, etc.

Furthermore, the pressure variations recorded at central sites are greater than those recorded peripherally. Thus, according to Fig. 5, the former may lie in the nonlinear part of the curve (vessel-wall distortion).

IV. THE COURSE OF THE VESSEL

We can largely abolish the deformation by measuring the pressure directly with a needle connected to the proper electronic recording device, but the disadvantage of performing a surgical procedure is obvious. Another method which might be tried involves the use of a small, blunt piston with a stiff spring which may be pressed into the skin and vessel wall, thereby obtaining a displacement of the vessel wall proportional to the pressure change. The vessel wall, subcutaneous and cutaneous tissue, and the stamp, form in this case a system with a resonant frequency far above 30 cycles per second. Also, because of the large stiffness factor ("restoring force") of the springs, the excursions of the stamp are small, so that linearity exists. Even if this succeeds, the pressure curves measured centrally differ from those measured peripherally. This deformation cannot be eliminated, because this distortion occurs as the wave travels from central to peripheral segment (e.g., brachial to radial segment). It appears that each part of the vessel passed by the wave forms with the surrounding tissues a vibrating system (just like the tambour) with resonant frequencies less than 30 cycles per second. Further deformation results from wave reflection against arterial branches and against the "periphery." Thus, if we assume that the maximum points of two curves measured along an arterial segment are "equal," the velocity computed from the measured distance is not at all a good approximation to the "true velocity." In all cases we find two different results when maxima and foot-points are used respectively.

V. INFLUENCE OF FREQUENCY

Even if we could assume that the vessel wall and surrounding tissues were constant, deformation would still result from the fact that different harmonics of the pulse wave are propagated with a different velocity. This gives a phase shift, and the end result is a deformed peripheral curve.

VI. ALINEARITY OF DIFFERENTIAL EQUATIONS

Suppose that we made the pressure at the first part of a straight, isotropic (homogeneous) tube vibrate in simple harmonic motion, so that there was only one frequency. Still, deformation would occur, but not deformation in the strictest sense of the word. The cause of the "deformation" here is due to the fact that, on theoretical grounds, the pulse wave does not exist! The wave would exist if certain terms in the differential equations of motion could be neglected, i.e., the products of displacements of particles in the fluid, the vessel walls and their derivatives with respect to the displacements themselves. If this neglect is allowed, the approximation may be too rough, but it is only in this way that a solution of the differential equation can be derived having the form of a phe-

nomenon which has a velocity of propagation, i.e., P = f(x − ct). For, from

$$f(x_0 - ct) = f\left\{x_1 - c(t + \frac{x_1 - x_0}{c})\right\} = f\left\{x_1 - c(t + \tau)\right\}$$

we see that the pressure in a point x_0 at a time, t, will be the same $\tau = \frac{x_1 - x_0}{c}$ seconds later at some other point, x_1, so that $c = \frac{x_1 - x_0}{\tau}$ can be termed the velocity of propagation of the pressure. Thus, there is pressure-wave propagation if we are allowed to neglect the terms mentioned above. Without neglecting these terms, the solution of the differential equation has the general form P = f(x, t), i.e., the two independent variables x and t cannot now be unified into one single, independent variable, Y, defined by Y = x − ct, and so a velocity of propagation need not exist, for it is unlikely that a number, c, can be found so that at every point x_1, the relation

$$f(x_0 , t) = f\left\{x_1 , t + \frac{x_1 - x_0}{c}\right\}$$

is fulfilled. If we plot f (x − ct) at two different times as a function of x, we get two identical curves. They are only displaced with respect to each other along the axis of x. However, if we plot f (x, t) at two different times, we get two curves that may differ totally.

Hence, on theoretical grounds there is no true pulse-wave propagation, and we are forced, therefore, to define the pulse-wave velocity empirically. We must, for example, say that the two foot-points (Fig. 2) are by definition corresponding points, and that the velocity is equal to the distance, $x_2 - x_1$, divided by the time, $t_2 - t_1$. There is little wonder that when two other points are considered, totally different "velocity" values are obtained, even negative values in some cases.

VII. DIFFERENT MODES OF VIBRATION

Suppose we consider another problem: In considering tubes in which the displacements are small and their products are therefore negligible, there is still deformation. To demonstrate: If a simple harmonic oscillation is transmitted through an isotropic tube, longitudinal, torsional, and flexural waves can all be produced, each with its own velocity or velocities. It is thus probable that two wave forms exist simultaneously, and because of their velocity difference these waves will shift in relation to each other as they course through the tube. The end result is a wave exhibiting an entirely different form, i.e., deformation.

VIII. EXPERIMENTS

Since we know that something like a pulse wave exists, in spite of the absence of a theoretical basis, there must be, roughly speaking, a self-propagating phenomenon. So, the prerogative of neglecting certain terms in the differential equations is not totally absurd. Experimentally, the pulse-wave velocity has been measured by many investigators, but the results are not hopeful. The spreading of values in normal persons is so great that if in an arteriosclerotic person a large velocity is recorded, one may not conclude that wall rigidity was

the cause. Spreading may originate from any of three causes: (1) measuring apparatus, (2) deformation, as discussed above, and (3) condition of the person, such as meals (see Table II) and respiration. The velocity on one day may be ± 20 per cent greater on the next day in the same person. The measuring apparatus and the condition of the person can certainly be improved upon, but little if any improvement can be expected in regard to deformation.

It is still possible to conceive that determinations of pulse-wave velocity may be performed at some time in the same individual so as to study the influence of therapeutic measures. It is also quite possible that the study of certain wave characteristics may have clinical importance.

The uncertainty raised by the possibility of deformation of the pulse wave can be seen in the tables below.

A. *Deformation of the Curve.*—We see from Table I that: (1) The velocity in the old man is significantly greater than that in the boy. (2) The velocity in the boy did not differ in the two arterial segments, but in the old man the velocity in the brachium was twice that in the antebrachium. Calcification could be responsible but deformation is also a likely cause.

TABLE I

SUBJECT'S AGE	BRACHIUM	ANTEBRACHIUM
	VELOCITY AND STANDARD ERROR (CM./SEC.)	VELOCITY AND STANDARD ERROR (CM./SEC.)
11 years 80 years	955 ± 35 2,470 ± 200	895 ± 87 1,330 ± 62
Quotient	2.6	1.5

Fifty measurements were made in each subject.

B. *Condition of the Patient.*—

Meals: In Table II the influence of meals is recorded in an 11-year-old boy. From the table it is noted that after a meal there is a significant change in pulse-wave velocity in peripheral vessels. This is not true for the aorta. The reason for this is not known but one can theorize that immediately after a meal there is peripheral vasoconstriction with vasodilatation in the splanchnic area. From

TABLE II

AORTA		LEG		BRACHIUM		ANTEBRACHIUM	
WITHOUT MEALS	WITH MEALS	WITHOUT MEALS	WITH MEALS	WITHOUT MEALS	WITH MEALS	WITHOUT MEALS	WITH MEALS
436 ± 13	423 ± 8	806 ± 10	1,028 ± 18	955 ± 23	1,460 ± 46	890 ± 87	1,111 ± 42

Young's classic formula

$$Vel = \frac{DE}{2\rho r}$$

where D = wall thickness, E = Young's modulus, r = radius of the tube, ρ = density of the blood, one can see that an arterial constriction could affect the wave velocity (D and E supposed constant).

Respiration: If inspiration is held for about half a minute, quite often there is an increase of 30 per cent or more in the pulse-wave velocity. The respiratory influence is especially manifest in peripheral vessels. Because the effect of a meal and respiration is smaller in the aorta, that vessel is perhaps preferable for measurements of the pulse-wave velocity.

SUMMARY

The methods employed in the measuring of pulse-wave velocity are subject to gross error because of alinearity and frequency distortion resulting from low-resonance frequencies of instrumentation and arterial segment and extraneous tissue interference. Deformation also occurs because of different speeds of propagation of the various pulse harmonics.

Some examples are presented showing the effect of meals on the pulse-wave velocity. Respiration also has a great influence.

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Some Clinical Notes on Patients With Mitral Valvular Disease Who Have Had Mitral Valvuloplasty. Part I

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INTRODUCTION

The purpose of this study is to analyze some of the clinical features in cases of rheumatic mitral valve disease which were present before and after cardiac surgery, in order to help in the selection of patients and to try to appraise the amount of benefit that may be expected from surgery at different stages in the progress of mitral valve disease.

Although there are only 72 patients in this study, they all have been seen before and followed after surgery by one (S.A.L.) or both of the authors. The general appraisal of the problem concerned the degree of preoperative disability and postoperative improvement; these have been judged entirely on the basis of personal and clinical observations. This may have an advantage, as it is sometimes thought that a surgeon has a natural bias in estimating the benefits from his surgery. All these patients have been operated on at the Peter Bent Brigham Hospital; Dr. Dwight E. Harken performed the operations on all but five of the patients, these latter being operated upon by Dr. Harrison Black. No discussion will be made concerning catheterization findings or involved observations of circulatory dynamics. In fact, only a few such observations were made in this group of cases. Inasmuch as physicians are dependent, for the most part, on simple clinical methods to guide them, this general point of view was maintained throughout this study. In the great majority of instances the diagnosis of the valvular lesion and the advisability of surgery will have to be, and can be, made using the comparatively simple methods that are available in most hospitals. Cardiac surgery has grown so much in its extent that, when the enormous number of valvular cases is added to the smaller but important group of congenital cases amenable to surgery, it cannot be limited to a small number of surgical centers. There is a great need for competent and properly trained cardiac surgeons to carry on this work in more and more of the hospitals of this country and all over the world.

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The heart has been the last organ of the body to be treated surgically. There have been obvious reasons for this. Apart from the inherent difficulties of manipulating an organ that is in constant motion, there has been evident fear of cardiac arrests or irreversible and disastrous damage to such a vital organ. At first, simple traumatic injuries to the heart muscle were repaired in isolated and dramatic instances. Then, diseases of the pericardium were treated surgically under certain circumstances. The interior of the heart, however, remained unapproachable.

In 1923, the first case was reported in which mitral stenosis was directly attacked through the ventricle in the hope of enlarging the valve.[1] Although this patient seemed to improve for several years, subsequent similar cases operated on failed to survive the operation, and therefore this procedure was abandoned. Although in 1925, Souttar[2] reported another isolated case operated on through the auricular route, it was not until 25 years later through the simultaneous efforts of Harken,[3,4] in Boston, and Bailey,[5] in Philadelphia, that rheumatic valvular disease became a problem of general surgical interest. In retrospect, one may explain the long delay between the first case in 1923 and the more recent era beginning in 1948 by four factors. In the early period, antibiotics were not available; the threat of infection, therefore, was ever present. Second, there were no blood banks, and so the means to combat an overwhelming hemorrhage were not at hand. Third, the science of anesthesia, including the various ways of treating sudden operative cardiac arrhythmias or arrests, had not been developed to its present high level. Finally, the approach through the auricle greatly simplified the procedure. It is fair to say that the time was not quite ripe in 1923 to attack such a difficult problem with a sufficiently low operative mortality.

Apart from all this, in former years there was a strong impression, held until very recently, that the valvular defect of rheumatic heart disease was unimportant or immaterial. It is little appreciated by the present generation of physicians that, even after the turn of this century, some leading cardiologists believed that the fate of the patient with rheumatic valvular disease did not depend on the degree of constriction or incompetency of the valve, but mainly on the state of the heart muscle. In fact, when a reprint of the first case of mitral stenosis to be operated on was sent to Sir James Mackenzie by one of us (S.A.L.), his reply indicated this general point of view. The following quotation from this letter might be of historical interest. "The suggestion for slitting up the stenosed mitral orifice was put forward by Lauder Brunton some twenty-five years ago, and I gave it some consideration then. My reasons for not pursuing the subject were, in the main two-fold. First the tissue is of the nature of scar tissue, and when scar tissue is cut it speedily re-unites and the condition for which it was done is only temporarily relieved. Second, the heart failure that arises from mitral stenosis is not entirely due to the valve lesion, and in many cases due to the damaged muscle."* To some extent this was a continuation of some heated discussions one of us had with him and Sir Thomas Lewis some years before,

*A letter written by Sir James Mackenzie, Oct. 15, 1923.

in 1917. The unimportance of the valvular component in rheumatic heart disease was a view held in England, and to a lesser extent in the United States, for a good many years. It is also reflected in the following quotation from a publication of Lewis'[6]: "There is no evidence to show that any valve defect imposes a burden on the healthy heart which even in the absence of intervening hypertrophy will result in the heart's failure." The diametrically opposite view was expressed in a more recent publication entitled "The Great Importance of Valvular Injury in Rheumatic Heart Disease."[7] It is against this historical background that the development of modern cardiac surgery is to be viewed.

The preoperative clinical status of patients with mitral stenosis was divided into four groups: Group I consists of patients who had no symptoms whatsoever. It is usually inaccurate to say that the patient's mitral stenosis is entirely symptomless. It is only rarely that one sees a patient with unequivocal mitral stenosis who can run foot races or climb mountains without more than the normal difficulties. There are many, however, who can carry on ordinary, moderate duties and can be entirely unaware that they have anything wrong with their hearts. Such patients can swim and dance, play ordinary games, climb stairs, and the like without feeling any more uncomfortable than the normal person. No patient who belongs to this group was included in this study, since in none would surgery have been advised. Mitral valvular surgery has not as yet become so simple and innocuous and the prognosis in rheumatic valvular disease has not reached the stage of such accuracy that there is any justification for recommending an operation as a prophylactic measure in patients who are still quite fit, able to work, and are little if at all embarrassed. There are still large numbers of patients who do well for decades without any special medical care.

In Group II are included those patients who have had no symptoms at rest, but who do have slight limitations on ordinary effort. They might be troubled with palpitations or breathlessness or weakness on walking a flight or two of stairs or on hurrying in the street. They are generally able to walk considerable distances on a flat level at a slow or moderate pace, even though they cannot hurry. They have no objective evidence of congestive failure. They may have had transient arrhythmias, like paroxysmal auricular tachycardia or auricular fibrillation, but they do not have persistent auricular fibrillation.

Group III includes those patients who have significant symptoms on slight effort. They cannot go up one flight of stairs without considerable difficulty, nor can they walk many blocks in the street on a flat level. They may or may not have had objective evidence of congestion such as peripheral pitting, engorged liver, râles at the bases of the lungs, or hydrothorax. The evidence of heart failure generally has been responsive to cardiac therapy, either entirely or for the most part. The presence of persistent auricular fibrillation or the evidence of previous gross arterial emboli would automatically place the patient in Group III. The same is not necessarily true in cases of acute pulmonary edema or hemoptysis, unless these conditions are recurrent. If these conditions were rare or isolated and other features of the case were favorable, the patients could still fit into Group II.

In Group IV are included all seriously ill patients who have had irreversible gross heart failure, some with cardiac cachexia and others with multivalvular heart disease. These four groups correspond roughly, but not entirely, to Class I, II, III, and IV of the "Nomenclature and Criteria for Diagnosis of Diseases of the Heart" of the American Heart Association. There were other considerations such as the age, sex of the patients, the presence or absence of visualized calcification of the valve, etc., that influenced the determination of the classifications in some instances.

It was stated above that in both the selection and the estimation of the results obtained, a "clinical" appraisal was employed. This may seem to be a vague and inaccurate method of judgment. In order to obtain fine measurable differences in the dynamics of the circulation, it would have required elaborate catheterization studies conducted before operation and at various intervals after the operation. This would have entailed considerable work, more than was planned in this study, and to some extent would have been a greater hazard to the patient than the results might have merited. Certain information could be obtained by such studies, but it is not certain that any greater accuracy in determining the clinical progress of the patient would have been made possible. In any event, most cases will have to be followed by the average practitioner and internist without elaborate methods of investigation. After becoming familiar with the various ups and downs that occur in the progress of rheumatic valvular disease, one becomes fairly well equipped to judge the changes which are to be expected in many of these cases. Unpredicted events, both favorable and unfavorable, still take place. Such events as the development of subacute bacterial endocarditis, the disastrous occurrences of peripheral arterial or pulmonary emboli, the subsidence of smoldering active rheumatic infection, the development of coronary artery disease, all may obviously change the outlook. Complicated preoperative and postoperative studies would help little in enabling one to predict these possibilities or to aid in their prevention.

To estimate the change in the clinical status that resulted from the operation was not simple. It could be determined by appraising the subjective and objective findings after operation with those present before operation, taking into account what might have been logically expected to occur during the ordinary course in that interval of time. Some improvement is to be expected from the medical management of the cardiac during the hospital stay. Some patients gain considerably from the psychological boost that is involved in a procedure as dramatic as a heart operation. They often expect a great gain, and some like to exaggerate their sense of well-being and minimize their discomforts in order to please the surgeon or the physician, or out of gratitude for the fact that they have survived the operation. Only when they are closely pressed for details does the truth become clear. What may be found is that they feel better than they did the first several weeks after the operation when their condition was rather poor. If asked whether they are any better than they were before the operation, whether they can now do things that they could not perform before the operation, some of these patients will admit that they have not quite reached or, at least, have not surpassed their preoperative level of activities.

Subjective symptoms and the general appearance and behavior of the patient, although less definitive and more difficult to measure, are a still more valuable guide as to the progress of these cardiac patients than are objective findings. A patient who has been confined to her home or to life in a bed and chair is much more impressed by a change that enables her to go out to do some shopping, visit friends, or go to the theater, than she is by an increase or decrease of the transverse diameter or the heart. To be sure, objective data could be more easily followed, but their value depends on the interpretation placed on them, and that is no simple matter. It is reasonable to suppose that the disappearance of pitting edema or enlarged liver would be desirable changes to observe. However, most of the physical findings have been disappointing as guides to the progress that was taking place. Marked improvement occurred with no change in the heart size or vital capacity of the lungs or the intensity or character of the murmurs. A further point that must be considered after a lapse of months or years is to be aware of what might have happened during that interval of time had no cardiac surgery been performed. As the years pass, if the patients are as well but no better than they were before the operation, one might say that they survived this interval of time only because of the operation, and that they would have deteriorated or died long since on ordinary medical management. This latter concept was not considered in analyzing the cases, except in rare instances. Another type of progress that is difficult to analyze is that of restenosis after operation on the mitral valve.

There are certain complications in rheumatic valvular disease that are difficult to analyze. If a patient had arterial emboli or frequent attacks of pulmonary edema or hemoptysis before the operation and none afterward, can we ascribe the beneficial results to the surgery? In so far as the occurrences of arterial emboli are concerned, and especially of cerebral emboli, there is an important statistical factor to keep in mind. It seems that in the natural course of events, cerebral emboli, with passing of the years, decrease in frequency after the onset of auricular fibrillation. From this it would follow that during the third, fourth, or fifth year after the beginning of auricular fibrillation, even without surgical intervention, cerebral emboli would be much less frequent than during the first year. In the extensive follow-up study by Ellis and Harken[8] it was found that cerebral emboli were much less frequent postoperatively than preoperatively. The difficulty with this analysis is that, as has just been mentioned, during these advancing years emboli are much less frequent without surgery. Despite this it would seem that the incidence postoperatively is still much less than would be expected on medical management alone. Only after an appraisal had been made of all the clinical factors that could be assessed was final judgment rendered as to the degree of improvement, if any, that had resulted from the operation.

The most important single guide to the progress of these patients is their ability to breathe. The simple observation that a patient is able to walk greater distances without distress or without stopping, or that he is able to mount a greater number of steps, serves as a useful measure in deciding that the patient has improved. Therefore, one might have expected the vital capacity of the

lungs to be a reliable yardstick in following the progress of these patients. Ordinarily, cardiac patients with congestive failure show a decreased vital capacity of the lungs, and this almost always increases as the clinical condition improves under medical management. It was surprising to find in many of the cases in this study that the patient's ability to breathe improved markedly and that he was often able to make greater efforts without dyspnea although the vital capacity of the lungs remained the same or changed only slightly. This discrepancy is explained partly by the fact that there may be some mechanical restriction in the movement of the lungs that results from the operation itself. What is more important is that after a satisfactory mitral operation and the attendant relief of pulmonary congestion, although the vital capacity at rest may not have increased, the breathing space after effort may not fall as much as would have occurred before operation. In other words, the response to effort is the determining factor, because most of these patients have no dyspnea at rest even before the operation.

On the basis of operative results the survivors were classified according to change in clinical status as follows: *worse*, *unchanged*, *improvement slight*, *moderate*, *good*, or *excellent*. The various changes that took place after the operation were judged and classified after due consideration had been given as to how the patient felt or thought about his status and to the objective findings that we could detect on ordinary physical examination. The degree of improvement may well have been regarded as "good" in a patient who originally belonged to Group IV and was confined to home or existence in a bed and chair, if he were subsequently able to take short walks in the street, even if mounting one flight of stairs was still difficult. On the other hand, a Group III patient, in order to be regarded as having obtained a "good" result, would have had to be able to go up one or more flights of stairs without discomfort after operation. It is obvious that one would have to consider the preoperative level of disability in estimating the degree of improvement.

A further objective in following patients of this sort is an effort to gauge the time of maximum improvement and to determine how long it can be maintained. When mitral surgery was first generally undertaken, one naturally wondered whether the same rheumatic process which produced the original constriction of the mitral valve would continue to operate, with a gradual return of the original stenosis. It was inconceivable that the surgery could influence the underlying inherent mechanism that was responsible for the original narrowing of the valves. It seemed that all an operation would do was to set the "thermostat" back, and that it would gradually return to its original preoperative level. Sufficient time has already lapsed to make one feel that this is not necessarily true. The situation is somewhat similar to the problem of pericardial constriction. It is surprising to find that the mechanical removal of part of a pericardial scar around the heart has resulted in great and lasting improvement, when nothing had been done for the original cause of such a scar. Why did not the scar and constriction recur promptly? This has not occurred in many of the pericardial cases that have been observed for years, and the same seems already to be true

of many of the mitral cases. Furthermore, it has been observed in some of these mitral cases that improvement became even greater in the second or third year after the operation.

The reverse has also occurred, i.e., when an original improvement gave way to greater deterioration after one or more years. These changes in the clinical progress may result from variations in the degree of active rheumatic infection, the redevelopment of mitral stenosis after a period of improvement, or the complications that naturally take place in chronic rheumatic valvular disease. One extremely rare complication not observed in this study deserves special comment, inasmuch as it has been noted by one of us in a postoperative case in another hospital. This particular patient had been operated upon for aortic stenosis. During the following months, gradual severe and refractory right-sided heart failure developed, with considerable pitting edema, ascites, and increased venous pressure. The most likely explanation seemed to be pericardial constriction, which might have resulted from the presence of blood in the pericardium attendant upon the operation for aortic stenosis. With this in mind, an operation was urged and a diagnosis of pericardial constriction was confirmed. This is not a common postoperative complication because the pericardial cavity is generally drained, not permitting any lengthy presence of hemorrhagic fluid in the pericardial sac.

The appraisal of improvement cannot always be estimated during the early months after surgery. The so-called postcommissurotomy syndrome which resembles rheumatic reactivation might color the postoperative course. Even after these conditions have all cleared, it may take some time for favorable changes gradually to develop, such as a decrease in left auricular, pulmonary capillary, and pulmonary arterial pressures. It also may require a considerable time for the left ventricle that had been performing a decreased amount of work for years, with a small cardiac minute output, to hypertrophy and to adjust itself to the new dynamic situation.

One occasionally hears, especially from surgeons, that the patient was cured of the mitral stenosis. We doubt that this is ever accomplished by surgery even in those who obtain an "excellent" result. When improvement is great and there is no longer any dyspnea on ordinary effort, including stair climbing, it is very unlikely that vigorous running would be tolerated without difficulty. Likewise, in such patients with "excellent" results a certain degree of mitral stenosis is likely to persist even when at the end of the operation the surgeon estimated the mitral valve as very large, i.e., 4 sq. cm. or more. If the patient is to be regarded as no longer having mitral stenosis when classical signs are still present, there would be very little basis for making this diagnosis before operation. The classical signs of mitral stenosis generally persist even in those patients who obtain "excellent" postoperative results.

MATERIAL IN THE STUDY

The study consists of a review of 72 patients with mitral stenosis who were observed at the Peter Bent Brigham Hospital before and after mitral valvuloplasty. These comprise all patients subjected to surgery who were under the care of one of us. It is fair to say, however, that the

group is somewhat weighted in favor of the severer type of cardiac disability, particularly during the first few years, because a cardiac consultant is likely to have the more difficult problems under his care. Furthermore, during the first few years one was reluctant to subject to a serious surgical operation those cardiac patients who were not already gravely ill. As the operative mortality decreased, milder cases were more readily subjected to surgery.

There were 74 valvular operations performed in these 72 patients, 2 patients having had secondary operations at a later date. In 71 of the 72 patients, mitral stenosis of more or less severe degree was found at operation. In 1 patient no evidence of mitral stenosis was found, and this case, therefore, is to be considered as one of mistaken diagnosis.

The average age of these patients at the time of operation was 44 years. There were 61 females with an average age of 40.5 years and 11 males with an average age of 47.5 years. The age range for the females was 27 to 62 years, and for the males it was 39 to 60 years. It is of some interest that 9 patients in this series were over 50 years of age. During the more recent years some patients who might have been denied surgery in the earlier years have been operated upon.

The preoperative clinical status of all 71 mitral stenosis cases was divided into four groups. No patient who would fit into Group I (symptomless) was subjected to surgery. Group II (slight limitation on ordinary effort) included 19 patients, i.e., 26.7 per cent of the total. Group III (significant symptoms on slight effort) included 41 patients, i.e., 57.7 per cent of the total. Group IV (seriously ill with irreversible failure) included 11 patients, i.e., 15.5 per cent of the total. The average degree of preoperative clinical disability for the whole group was 2.9.

CLINICAL RESULTS

After having made the clinical diagnosis that mitral valvular stenosis is present, possibly in combination with mitral insufficiency or involvement of the other valves, the question foremost in the mind of the physician will be that of estimating the degree of stenosis in the particular case and the amount of benefit that can be expected from its repair. Are there any clues in the symptomatology, the physical findings, the x-ray, or the electrocardiogram that could guide one in advising operation? In an attempt to answer these questions, a careful analysis of the symptomatology, physical findings, x-ray findings, and electrocardiograms of all the patients in the various groups was made in relation to the results obtained by surgery.

There were 6 operative deaths among the 72 patients who had 74 operations, i.e., 8.1 per cent. Three were males and 3 were females. When it is realized that there were 61 females and only 11 males in the entire series, although these numbers are very small, the general impression is that males do less well than females. There were 5 deaths (1 male and 4 females) among the 66 remaining patients during the follow-up period. There were 7 whom we were unable to contact for re-examination, although they were known to be alive. The follow-up period was 42.0 months.

The average age of the 6 operative fatalities was 45.8 years. This is about 5 years older than the average age of those who survived the operation (41.0 years). Two of these 6 belonged to Group II, 1 to Group III, and 3 to Group IV. The average degree of preoperative clinical disability of these 6 patients was 3.3, which was definitely higher than for the 66 patients who survived the operation (2.8). Although the immediate operative mortality, as indicated above, was 8.1 per cent, it must be emphasized that during the past 2 to 3 years the figure has fallen to about 1 per cent in this hospital for patients in Group III.

The 5 patients who died postoperatively survived for periods ranging from 2 months to 7 years, with an average of 36 months. The average age of these patients was 43.4 years. These five belonged to Group III, as to preoperative clinical disability, the average being 3.2. The average age at the time of operation of the remaining 61 patients, all of whom were known to be alive, was 39.9 years.

The change in the clinical status after operation, as mentioned above, has been indicated in the following manner: worse, unchanged, improvement (1) slight, (2) moderate, (3) good, (4) excellent. There were, therefore, four degrees of improvement, 1 to 4. For the purposes of this discussion, a figure such as 2.5 would indicate a degree of improvement between moderate and good.

Among the 58 patients there were 3 who were considered as worse after the operation, 5 who were unchanged, 7 who had grade 1 improvement, 12 who had grade 2 improvement, 24 who had grade 3 improvement, and 7 who had grade 4 improvement. The average degree of improvement was 2.3 and the average follow-up period was 42 months. The average follow-up period varied somewhat in the various groups from about 3 to 5 years. It is of interest, however, that those with the maximum improvement (grades 3 and 4) have already been followed for about 4 years. There was very little difference in the improvement between those who were in preoperative severity Group II and those in Group III, the average degree of improvement being 2.4 and 2.2, respectively. The worst group, however, (Group IV severity) did obtain less postoperative improvement (only 1.8).

It was of interest to determine the average length of follow-up for the patients of different degrees of preoperative severity. The average postoperative period of follow-up for the 15 patients with Group II severity (in whom the information was available) was 37.0 months. For 32 patients with Group III preoperative severity it was 42.3 months, and for 7 patients with Group IV severity it was 53.8 months. It is obvious that the follow-up period was adequate in all three groups. It is also of interest that the follow-up period was longest in the more severely ill patients. This is explained by the fact that in the early years of mitral surgery, only patients who were markedly disabled were subjected to operations. In more recent years, as the surgical risk lessened, cases with slighter disability were operated upon.

From this study it is clear that surgery for mitral stenosis can be carried out with a decreasing operative risk that is now comparable to the operative risk of major abdominal surgery. It is also evident that the results on the whole are satisfactory, that improvement is to be expected in the great majority of cases (although not in all), and that, generally, this improvement can be maintained for some years. The degree of improvement varies in different cases, but even those cases with marked disability (Group IV) not infrequently show strikingly beneficial results. An analysis was made of various clinical factors that might have a bearing on the selection of cases and help in predicting favorable results from surgery. Many of these points have been carefully studied in the past by other observers.[9,10]

BLOOD PRESSURE

The relation between the blood pressure level and the various clinical features was ascertained. The cases were divided into four groups, A, B, C, and D. Group A contained those with preoperative systolic blood pressure readings of 129 mm. Hg or less (42 cases). Group B contained those with readings of from 130 to 149 mm. Hg (19 cases). In group C were those with readings of from 150 to 179 mm. Hg (6 cases). In group D were those with readings of 180 mm. Hg and over (4 cases). For some of the analyses, the lower two and upper two were grouped together, because otherwise the numbers were too few. The degree of improvement showed a steady decline from group A to group D as the blood pressure increased, the degree of improvement being expressed by the figures 2.6, 2.3, 1.3, and 0.7, respectively.

Among the 61 patients belonging to the first two groups without hypertension there were 3 immediate operative deaths and 3 late deaths. In contrast, there were 3 operative deaths among the 10 belonging to groups C and D, and 1 late death. To be sure, those with lower pressures were somewhat younger than those with higher pressures, the average ages being 40.1, 42.3, 46.8, and 47.0 years, respectively, in the four groups.

It has been thought that patients with hypertension and mitral stenosis often did fairly well and, in fact, somewhat better than those with the same degree of disability and a lower pressure. Elderly women with mitral stenosis and auricular fibrillation often seemed to have had hypertension.[11] It seems reasonable to suppose that it would be difficult to maintain a markedly elevated blood pressure with a tight mitral stenosis and the necessarily decreased cardiac output. For this reason, it was suspected that a larger mitral valve would be found at the time of operation in cases with elevated blood pressure than in those with normal readings. This suspicion proved to be true in the present study.

The valve size was estimated by the surgeon at the time of his exploration. Those described as 0.5 sq. cm. or less (11 cases) were classed as "very tight," those from 0.6 to 1.0 sq. cm. as "tight" (43 cases), those over 1.0 sq. cm. as "moderate" (12 cases); the others comprised the group in which the surgeon described the valve as predominantly incompetent, with only slight stenosis (4 cases). (In one case the valve size was not described.) Among the 10 cases with hypertension (blood pressure groups C and D) there was not one with a very tight valve. Five were tight, 4 were moderately tight, and 1 was predominantly incompetent. Of the remaining 60 cases, in which the blood pressure was under 150 mm. Hg, there were 11 cases of very tight mitral stenosis, 38 tight, 8 moderately tight, and 3 primarily incompetent. It is rather striking that when hypertension was present, there were *no* very tight valves. In fact, of the 11 instances in which the stenosis was very tight (0.5 cm. or less), 10 belonged to blood pressure group A, i.e., blood pressure under 130 mm. Hg.

The relative antagonism between very tight mitral stenosis and marked hypertension is confirmed by a further analysis. There were no hypertensive patients among the 11 cases with very tight mitral stenosis and only 5 hypertensive patients among the 43 cases with tight mitral stenosis. In contrast, there

were 5 hypertensive patients among only 16 cases with "moderate" mitral stenosis or those with predominant incompetency.

The level of the blood pressure had a slight effect on the expected improvement. The average reading of the 31 cases that showed grade 3 or 4 improvement following operation was 123.1 mm. systolic and 78.1 mm. diastolic, whereas corresponding readings for those 15 cases showing the poorest results (worsened by operation, no change or only grade 1 improvement) were 138.7 mm. and 85.2 mm. Hg. It would appear then that increase in blood pressure makes the prospects a little less bright; however, it cannot be inferred that the pressure level itself is the determining factor. It has been shown that those with higher pressure levels are more likely to have a lesser degree of mitral constriction, and anatomical correction of this defect will therefore result in less gain.

AUSCULTATORY FINDINGS

The auscultatory findings that were present before and after surgery were noted by the same observer (S.A.L.). Immediately after operation, pericardial sounds obviously predominated, but after several days they vanished. The first comparisons of the basic cardiac findings were generally made about 2 weeks after the operation when bandages and stitches had been removed and the patient was ambulatory and feeling fairly comfortable. The heart sounds and murmurs were often somewhat decreased in intensity at this time. What seemed more important was to note any change that might have occurred some months later, when the patient might have already obtained a certain degree of improvement from the operation. For this reason, the main emphasis was placed on the findings obtained 6 to 12 months after the operation.

Apical Systolic Murmurs.—The relationship between the presence and intensity of murmurs to the degree of postoperative improvement was investigated. The intensity of murmurs was graded[12] in the customary fashion from 1 to 6. There were 19 instances amongst the 31 who had a favorable result (grades 3 and 4 improvement) in which no apical systolic murmur was heard, while there were only 4 out of 15 in the poorest group. Among the 31 patients who had grades 3 or 4 improvements the average intensity of the apical systolic murmur was 0.65; in contrast, for the 15 poorest results (worse by operation, no improvement or grade 1 improvement) it was 1.7. It is of interest that when each group (though small) was analyzed individually, there was a steady linear increase of the apical systolic murmur from the one with the greatest improvement to the one that was worst postoperatively.

In general, the apical systolic murmur was fainter than the diastolic in the favorable cases and the two tended to be of more equal intensity for the less favorable cases. There were, however, 6 exceptional instances in the favorable group in which the systolic murmur was definitely louder than the diastolic.

In the selection of patients, therefore, one tries to avoid those who have primarily mitral insufficiency and feels most hopeful in those with the least degree of this defect. The intensity of apical systolic murmurs has been one of the guides among many others that might indicate the degree of mitral incom-

petency. The so-called pure or tight mitral stenosis could be expected to show a diastolic rumble without any murmur at all in systole. Although there are exceptions in which tight mitral stenosis is associated with a systolic murmur, the reverse is very rare, i.e., appreciable mitral insufficiency as found by the surgeon during his exploration was very rarely observed where no systolic murmur was present preoperatively. The inference to be drawn is that the absence of an apical systolic murmur is fairly reliable evidence that significant mitral insufficiency does not exist. However, the presence of a systolic murmur of moderate intensity or louder is found occasionally where the mitral valve is considerably stenosed and regurgitation, if present, is of minor degree. In fact, the systolic murmur rarely is much louder (Grade 4) than the diastolic (Grade 1-2) when the valve is markedly stenosed. The exact mechanism of this anomalous finding is puzzling. It may be due to a minute mitral regurgitation through a very small opening during systole or it may possibly be a result of a tricuspid regurgitation and not due to mitral insufficiency at all.[13]

Mitral valvuloplasty in its present form is mainly meant to relieve the obstruction by a stenosed mitral valve. Concomitant mitral insufficiency, on the other hand, will be influenced only indirectly, if at all, by this operation. It has been demonstrated[14] that the coexistence of major mitral regurgitation and major stenosis is a physiological impossibility. With a marked obstruction of blood flow at the mitral valve there cannot be an increase in the volume of blood delivered to the left ventricle during each diastole. In fact, the volume would be less than normal. With each ventricular systole, if there were much reflux into the left auricle, there would be too little left to be propelled out through the aorta to maintain an adequate peripheral circulation. The physician, therefore, in order to exclude from operation those in whom mitral insufficiency seems to be the major component, will be presented with the problem of deciding in a particular case whether stenosis or regurgitation is predominant.

The systolic murmur is generally regarded as the most distinctive auscultatory finding of mitral insufficiency. It might be thought that the intensity of the systolic murmur could serve as a clue to estimate the degree of mitral insufficiency. This did not prove to be a completely dependable guide. There were very loud systolic murmurs (Grade 4) in patients who proved on operation to have had the most tightly stenosed valves (0.5 sq. cm. or less), and, on the other hand, there was one patient who proved at operation to have almost free regurgitation and only a very minor degree of mitral stenosis and yet presented preoperatively only a faint systolic murmur (Grade 1).

A calculation of the average intensity of the systolic murmur in the 3 groups of "very tight," "tight," and "moderately tight" stenosed valves gave the following results. The average intensity of the systolic murmur in 11 cases with very tightly stenosed valves was 1.3, in 42 cases with tightly stenosed mitral valves it was 1, in 12 cases with moderately tight mitral stenosis it was 1.6, and in the 4 cases that proved to have free regurgitation it was calculated to be 3. Notwithstanding the variations discussed above, the systolic murmur, in general, is louder with more marked mitral insufficiency. However, a faint systolic murmur does not at all exclude the possibility of a marked or even pre-

dominant mitral insufficiency; likewise a very loud systolic murmur does not exclude a very tight mitral stenosis with only minor mitral insufficiency. In these cases decisions will have to be made on additional data.

It is of interest that the average improvement in those few cases with a Grade 4 or louder systolic murmur proved to be almost as good (2.2) as in those that showed no systolic murmur at all (2.6). This is in accord with the correlation reported above that a very loud systolic murmur can occasionally be observed in very tight mitral stenosis. It seems, therefore, that the most promising cases (all other factors being favorable) are those with no systolic murmur at all and possibly those with very loud systolic murmurs.

When the patients were re-examined 6 to 12 months postoperatively, the systolic murmur was found to have increased on the average 1.9 as compared to the preoperative findings in 16 cases. It remained unchanged in 27 cases and was decreased in 5 cases on the average 1.2.

It is of considerable interest that all those in whom the systolic murmur increased in intensity or appeared anew after the operation had a decidedly poorer result from the operation than those in whom the systolic murmur remained unchanged or decreased after the operation. The average improvement for those who had an increase in the systolic murmur postoperatively was only 1.6 (slight to moderate); whereas, in those in whom the systolic murmur remained unchanged the average degree of improvement was 2.9 (marked improvement), and in those in whom the systolic murmur decreased in intensity following the operation the average degree of improvement was 2. The appearance postoperatively of a systolic murmur or the intensification of a pre-existing one, therefore, is not a favorable sign.

Exceptional Cases With Systolic Murmurs.—There were 6 instances in which the finding of a fairly loud apical systolic murmur might have led the examiner to feel that there was a sufficient degree of mitral regurgitation to contraindicate surgery for mitral stenosis. In these 6 cases, however, operation resulted in a very satisfactory improvement, i.e., grade 3-4 results. There were other patients with fairly loud apical systolic murmurs who had less favorable results from surgery. The question quickly arises whether there are some clues that might enable the physician to predict which mitral patients might still do well though they show a Grade 3 or louder apical systolic murmur.

CASE 1.—A. B., a 55-year-old woman, was quite sick with objective evidence of right- and left-sided congestive failure. There was a Grade 4 apical systolic murmur and a Grade 2 apical diastolic murmur. ECG showed right ventricular hypertrophy. The mitral valve was found at operation to be fairly tight (less than 1 sq. cm.). She has maintained a most satisfactory result for 4 years.

CASE 2.—I. C., a 39-year-old woman, had considerable dyspnea, a history of occasional hemoptysis, probably acute pulmonary edema. Heart was regular and showed a Grade 3 apical systolic murmur and only a questionable, faint diastolic murmur. The heart was considerably enlarged (42 per cent above average). The ECG showed right ventricular hypertrophy and P-mitrale. The patient has maintained a most satisfactory improvement (grade 3) for 4½ years since her valvuloplasty.

CASE 3.—S. K., a 47-year-old woman, had considerable dyspnea and recurrent attacks of pulmonary edema. Heart showed a Grade 3 systolic murmur and an almost equally loud apical

diastolic murmur. ECG showed right ventricular hypertrophy. The mitral valve was found at operation to be 0.6 sq. cm. The patient has maintained a satisfactory improvement for 4 years since operation, despite the fact that permanent auricular fibrillation developed directly after surgery.

CASE 15.—C. M., a 43-year-old woman, belonged in the most severely ill group (Group IV). She had irreversibie right heart failure with a huge liver, marked cardiac enlargement (43 per cent above average), showed a Grade 3 apical systolic and only a Grade 1 diastolic murmur. The ECG showed auricular fibrillation and right ventricular hypertrophy. The valve size at operation was found to be 0.5 sq. cm. This patient has maintained a markedly improved result (grade 3) for 1½ years.

CASE 30.—M. V., a 33-year-old woman, had distressing dyspnea and spells of pulmonary edema with occasional hemoptysis. There was a Grade 3 to 4 apical systolic murmur and a faint Grade 1 diastolic murmur. The ECG showed normal sinus rhythm, right ventricular hypertrophy, and P-mitrale. The heart was 25 per cent enlarged. The mitral valve was found at operation to be 0.5 sq. cm. in area. Patient had the best kind of result (grade 4 improvement) which has been maintained for 4 years.

CASE 48.—J. H., a 38-year-old woman, was quite short of breath, the liver was enlarged 3 fingers below the costal margin, and the heart showed a Grade 3 systolic and a Grade 2 diastolic murmur at the apex. The heart was moderately enlarged (30 per cent). The ECG showed right ventricular hypertrophy, normal sinus rhythm, and P-mitrale. The valve at operation was found to be 0.4 sq. cm. in area. Patient was known to have obtained a marked improvement for at least 6 months.

The outstanding characteristics of these patients who showed considerable or marked mitral stenosis at operation and manifested a fairly loud apical systolic murmur were that they were all female, that they all showed right ventricular hypertrophy in ECG, and when normal sinus rhythm was present, a P-mitrale was found. (For criteria of RVH see later in ECG section, Part II.) Most had pulmonary edema or hemoptysis. Favorable results were therefore obtainable when the heart was considerably enlarged, when the liver was also considerably enlarged, and even when the congestive heart failure had been irreversible on medical management.

Apical Diastolic Murmur.—It is well known that the apical diastolic or presystolic murmur is the most distinctive feature of mitral stenosis. It is often thought that a louder diastolic murmur means a greater degree of mitral stenosis. This did not prove to be true in this study. There were loud and faint diastolic murmurs with slight stenosis and the same was true for the cases with marked stenosis. In fact, there were several instances of "very tight" or "tight" mitral stenosis in which no diastolic or presystolic murmur whatever could be heard at the apex, and the diagnosis of mitral stenosis had to be made on other criteria. It so happened that there was no instance without a diastolic murmur among those who had only a "moderately" narrowed valve (over 1 sq. cm.).

A calculation of the average loudness of the diastolic murmur in the 3 groups ("very tight," 0.5 sq. cm. or less; "tight," 0.6 to 1.0 sq. cm.; and "moderately tight," over 1 sq. cm.) was of some interest. The average intensity of the diastolic murmur for the 11 cases with a "very tight" stenosis was 1.6; for the 43 cases with "tight" mitral stenosis it was 2.4; and for the 12 cases with "moderately tight" mitral stenosis it was 2.1. It would appear, therefore, that the diastolic murmur can become fainter with the extreme degree of mitral stenosis, and in rare instances might even be absent. Apart from this it must also be ap-

preciated that a rather loud diastolic murmur can be present in cases with primarily mitral regurgitation having a patulous mitral valve with a slight diaphragmatic-like stenosis of the entire ring. Only a few such cases were found in this study, as they would not have been chosen for operation for mitral stenosis.

It was of interest to correlate the loudness of the diastolic murmur observed preoperatively with the ultimate improvement achieved postoperatively. Three patients with no diastolic murmur preoperatively had an average grade 2 improvement (moderately improved). In fact, one of these three had a grade 3 improvement. Two more patients with no diastolic murmur preoperatively died at the time of the operation or immediately thereafter. Ten patients with a Grade 1 diastolic murmur had an average improvement of 2.4 (moderate to marked). Twenty-two patients with a Grade 3 diastolic murmur had an average improvement of 2.2 (moderate to marked) and, finally, 2 with a Grade 4 diastolic murmur showed a 3.5 improvement. An analysis from a different angle gave similar results. The intensity of the diastolic murmur for the 2 groups (3 and 4) that obtained the best results (31 cases) was 2.4, and for the 15 poorest results (worse, unchanged or grade 1 improvement) it was 1.9. A louder diastolic murmur may, therefore, indicate a slightly greater expectation of a good result.

When patients were re-examined 6 to 12 months after the operation, the intensity of the diastolic murmur was found to be decreased in 26 instances, about the same in 20, and slightly increased in 4. The decrease in intensity for the 26 cases was considerable as it averaged 1.7 (in the customary scale of 1 to 6). It is of further interest that, in general, those who had a greater reduction in the intensity of the diastolic murmur had a better clinical result from the operation. The average improvement for those who showed a decrease in the intensity of the diastolic murmur was 3.0 (marked improvement), while the degree of improvement in the remainder was 1.6 (slight to moderate improvement).

Basal Murmurs.—An analysis of the presence or intensity of basal murmurs, systolic or diastolic, in those patients who obtained a satisfactory result as compared to those with an unsatisfactory result reveals that there was very little difference in the two groups. It was often no simple matter to distinguish a diastolic murmur at the third intercostal space at the left sternal border, that might be called a Graham Steell murmur due to pulmonary insufficiency, from one due to aortic insufficiency. In a case of definite mitral stenosis, if there is satisfactory evidence of aortic stenosis (calcified aortic valves, loud aortic systolic murmur, plateau pulse, decreased aortic second sound with left ventricular hypertrophy in the electrocardiogram), a diastolic murmur at the left sternal border is best interpreted as aortic in origin. If these signs are absent, and there is no collapsing quality to the peripheral pulse and no high pulse pressure, the diastolic murmur at the left upper sternal border is best assumed to be due to pulmonary insufficiency. This general point of view is particularly valid if there is additional evidence of increased pulmonary arterial pressure such as right ventricular hypertrophy in the electrocardiogram, an accentuated pulmonary second sound, and an enlargement of the pulmonary artery. In this regard, an accentuated and somewhat delayed first sound in the second left intercostal

space ("the slatting sail sound") is a strong indication that the pulmonary artery is dilated. In a word, basal murmurs for the most part can be dismissed in cases of rheumatic valve disease if there is right ventricular hypertrophy in the electrocardiogram, when the question of mitral surgery has to be considered.

Accentuated Apical First Heart Sound.—An accentuated, snapping first heart sound at the apex is generally thought of as favoring the diagnosis of mitral stenosis. Intensity of the first heart sound was observed in these cases and described as normal, accentuated (Grade 1), markedly accentuated (Grade 2), and very markedly accentuated (Grade 3). In 12 out of 69 cases in whom this information was available, the first heart sound was not, or only questionably, accentuated. In 39 cases it was accentuated (Grade 1) and in 18 cases it was markedly or very markedly accentuated (Grades 2 and 3).

It seemed of interest to compare the degree of mitral stenosis as described by the surgeon during the operation with the degree of accentuation of the first heart sound as observed preoperatively. In 11 cases with a very tightly stenosed mitral valve, the average intensity of the first heart sound was 1.1; in 51 cases with a tight mitral stenosis, it was 1.2; in 11 cases with only moderately tight mitral stenosis, it was 1.1. It seems, therefore, that no prediction as to the tightness of the mitral stenosis can be made from the degree of accentuation of the first heart sound. In 4 cases with predominant mitral insufficiency and only minor mitral stenosis, the average intensity of the first heart sound was 1 (i.e., accentuated). Obviously from these 4 cases with predominant mitral regurgitation no conclusion can be drawn. The above observations of an increased first heart sound in these 4 cases with predominant mitral regurgitation does not invalidate the general concept that an accentuated first heart sound at the apex is fairly good evidence for mitral stenosis but also is present with predominant mitral regurgitation.

Calcification of the Mitral Valve.—In 25 cases in this group of 71, the mitral valve at operation showed some degree of calcification varying from very slight to very marked. When the degree of calcification is graded from i to iv, then 7 out of these 25 cases showed a grade i degree of calcification, 8 cases a grade ii degree, 9 cases a grade iii degree, and one case a grade iv degree of calcification.

The average intensity of the first heart sound in 23 cases with calcified mitral valves was 0.9; whereas in all other cases in which this information was available (43 cases) the average intensity of the first heart sound was calculated to be 1.3. It seems, therefore, that with calcified mitral valves the first heart sound is apt to be less accentuated than in those with noncalcified stenosed valves. However, in several instances where markedly calcified valves were found at operation, a markedly accentuated first heart sound had been observed preoperatively.

It was of interest to compare the clinical result obtained from the operation in cases with calcified valves and those with noncalcified mitral valves. Of the 25 patients with calcified mitral valves, 4 died at the time of the operation or shortly thereafter. Only 2 of the other 39 patients without calcified valves died at or immediately following the operation. The average clinical result from the operation in cases with calcified mitral valves was calculated to be 1.7 (i.e., slightly to moderately improved), and for those with noncalcified mitral valves

it averaged 2.2 (i.e., better than moderately improved). A calcified mitral valve seems, therefore, to present a greater immediate operative risk and the ultimate outcome in the survivors is slightly less favorable than in those with no calcification.

REFERENCES

1. Cutler, E. C., and Levine, S. A.: Boston M. & S. J. **188**:1023, 1923.
2. Souttar, H. S.: Brit. M. J. **2**:603, 1925.
3. Harken, D. E., Ellis, L. B., Ware, P. F., and Noonan, L. R.: New England J. Med. **239**:801, 1948.
4. Harken, D. E., Ellis, L. B., and Noonan, L. R.: J. Thoracic Surg. **19**:1, 1950.
5. Bailey, C. P.: Dis. Chest **15**:377, 1949.
6. Lewis, Sir Thomas: Diseases of the Heart, New York, 1937, The Macmillan Co., p. 144.
7. Levine, S. A.: The Great Importance of Valvular Injury in Rheumatic Heart Disease, Libro Homenaje al Profesor Doctor Ignacio Chavez, page 185. Editads por la Universidad Nacional Autonomia Mexico, 1945.
8. Ellis, L. B., and Harken, D. E.: Circulation **2**:637, 1955.
9. Wood, P.: British M. J. **1**:1051, 1113, 1954.
10. Likoff, W., and Uricchio, J. F.: J.A.M.A. **166**:737, 1958.
11. Levine, S. A., and Fulton, M. N.: Am. J. M. Sc. **186**:465, 1928.
12. Freeman, A. R., and Levine, S. A.: Ann. Int. Med. **6**:1371, 1933.
13. Schilder, D. P., and Harvey, W. P.: AM. HEART J. **54**:352, 1957.
14. Gorlin, R., Lewis, B., Haynes, F. W., and Dexter, L.: AM. HEART J. **43**:357, 1952.

Some Clinical Notes on Patients With Mitral Valvular Disease Who Have Had Mitral Valvuloplasty. Part II

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AURICULAR FIBRILLATION

It is well known that auricular fibrillation is a common late development in mitral stenosis. This arrhythmia may be transient in form, each spell lasting a few hours or a day or two; or in the course of time, and not infrequently with the first episode, it may become permanent. It may be arbitrarily regarded as a perpetual arrhythmia if it lasts a week or more; spontaneous reversion to normal sinus rhythm on digitalis therapy alone is rare after it has lasted this long.

Among the 71 patients in this study, 46 had chronic auricular fibrillation up to the day of the mitral surgery. The other 25 had normal sinus rhythms just before operation. Of the 25 with normal sinus rhythms, 8 developed auricular fibrillation during the operation or shortly thereafter. This change in rhythm may take place either during operation or one or two days later, or even as long as 10 to 12 days postoperatively. One of the 8 patients reverted to normal sinus rhythm spontaneously, and 1 other did so on digitalis therapy. In 3, regular rhythm was obtained on quinidine therapy. In the remaining 3, quinidine therapy was not successful, although in 2 of these, regular rhythm was obtained temporarily but auricular fibrillation quickly returned.

There were 4 among these 25 patients with normal sinus rhythm who had had previous bouts of auricular fibrillation which reverted preoperatively to normal sinus rhythm, either spontaneously or with the aid of quinidine. Three of these 4 with normal sinus rhythm at the time of surgery developed auricular fibrillation again during the operation or soon thereafter. In contrast to this, it is of interest to note that among the remaining 21 patients with normal sinus rhythm on the morning of the operation, only 5 developed auricular fibrillation during the immediate postoperative period. It would appear that those who had transient fibrillation in the past developed it more readily again during or directly after mitral surgery than did those who had not had it.

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The 46 patients who had persistent auricular fibrillation at the time of operation were maintained on constant digitalis; most of them were not given quinidine at all. In some, postoperative attempts were made to produce normal sinus rhythm, but these were generally unsuccessful. Occasionally, regular rhythm was obtained on quinidine, but the gross irregularity quickly returned. There were a few instances in which quinidine therapy failed before operation and succeeded several months after a successful valvuloplasty.

An important question that arises is whether to try to regularize the heart when auricular fibrillation is present before the operation is performed. It would seem best not to do this. The attempt is not likely to succeed if the auricular fibrillation has been chronic, and if it does succeed, the arrhythmia is apt to recur during the operation or shortly thereafter. One might just as well continue on digitalis therapy, keeping the ventricular rate at an appropriately slow level. The next question is whether to try, with the preoperative administration of quinidine, to prevent auricular fibrillation from developing as the result of the operation. The matter is debatable, for in the doses that might be required, untoward side effects would not be infrequent. There may be some justification for giving quinidine prophylactically in those patients who are known to have had transient auricular fibrillation in the past. When the arrhythmia is precipitated by the operation, there is justification for giving quinidine during the postoperative period, because of the likelihood that regularization can be obtained. However, in those who had chronic fibrillation before surgery, it is optional whether quinidine therapy should be attempted during the immediate postoperative convalescence or postponed for a few months. There are instances in which quinidine fails two weeks after satisfactory mitral valvuloplasty and succeeds even with lower doses a few months later.

ATTACKS OF PULMONARY EDEMA OR HEMOPTYSIS

There is a suggestive pattern among the cases of mitral stenosis that are prone to have recurrent attacks of pulmonary edema or hemoptysis. More often than not, the rhythm is apt to be regular, and the heart is only slightly enlarged or not more than moderately so, although the pulmonary artery may be quite prominent. Right-sided heart failure with enlarged liver and peripheral edema are striking by their absence. In some cases these features, no doubt, were present at the time when attacks of pulmonary edema and hemoptysis were occurring, but the patient carried on long beyond this and came to surgery when a more advanced stage had developed and the clinical features had changed.

There were 17 patients in this study who had attacks of pulmonary edema, 5 who had hemoptysis, and 9 who had both. Of 25 patients who had pulmonary edema in their past history, 12 had electrocardiographic evidence of right ventricular hypertrophy, 4 had combined ventricular hypertrophy, 8 had no ventricular hypertrophy, and 1 had a normal electrocardiogram. Among the 45 remaining patients, 23 had right ventricular hypertrophy, 10 had combined ventricular hypertrophy, 11 had no ventricular hypertrophy, and 1 had isolated left ventricular hypertrophy. It can be seen that there was no difference in the incidence of

right ventricular hypertrophy whether there was a history of acute pulmonary edema or not. It is of interest that among these 31 patients with pulmonary edema or hemoptysis, 17 had a normal sinus rhythm at the time of the operation and 14 had auricular fibrillation. Among the former there were some who had had transient bouts of auricular fibrillation, while among the latter there were at least 2 who were known to have regular rhythm until a very short time before the operations. A more detailed analysis of the type of rhythm that prevailed at the time when hemoptysis or pulmonary edema was occurring revealed that 23 (74 per cent) had a normal sinus rhythm at that time, and that only 8 (26 per cent) had auricular fibrillation. This proportion is in striking contrast to the findings in the other patients in this study, i.e., among the remaining 40, 8 (20 per cent) had normal sinus rhythms and 32 (80 per cent) had auricular fibrillation.

The clinical results obtained in this group of patients are, on a whole, quite satisfactory. Of the 31 patients, only 1 operative death occurred and only 1 patient died during the follow-up period. The degree of improvement among the survivors was 2.7, which is better than that in the remaining 40 patients who did not have hemoptysis or pulmonary edema. In the latter group the degree of improvement was calculated to be 2.1. Furthermore, in this latter group there were 5 operative deaths, and 4 additional deaths in the follow-up period.

There are some points of clinical interest in relation to this particular topic. Attacks of acute pulmonary edema in mitral stenosis do not appear to be so ominous as similar episodes observed in hypertension, aortic or coronary artery disease. There were quite a few instances in which attacks of pulmonary edema kept recurring over the course of many years. One striking instance which may be cited by way of illustration is that of a young woman who had had a great many attacks of pulmonary edema requiring morphine hypodermically over the course of 16 years. These attacks were precipitated by hurrying, dancing, coitus, alcoholic drinks, etc. She would show a regular cardiac rhythm and generalized râles during these spells, but after a prompt recovery, and in the intervals, the lungs were clear. She would then have very little dyspnea, and the vital capacity of the lungs would always return to a high level of 3,000 c.c. Throughout these many years she always had had a normal sinus rhythm. Only several weeks before her operation did auricular fibrillation appear.

One is not likely to see patients do so well, and for so long a time, after having had acute pulmonary edema while suffering from other forms of heart disease. There was another type of patient in which sudden attacks of dyspnea or pulmonary edema occurred as the direct result of the onset of auricular fibrillation. If this arrhythmia is paroxysmal, it may account for recurring attacks of pulmonary edema. In fact, when auricular fibrillation becomes permanent, paroxysmal dyspnea is not so likely to develop, especially if gross right-sided failure intervenes. Such patients may become increasingly breathless on effort, but the paroxysmal component disappears or becomes less prominent.

In discussing hemoptysis there is some confusion that cannot be easily clarified. The main interest here was in those patients who had brisk hemoptysis rather than slightly bloody sputum. The latter can come from general passive

congestion or pulmonary infarction. The former occurs from a different mechanism and resembles, in some respects, an epistaxis. Such brisk hemoptysis may result from dilated bronchial veins which develop in cases of mitral stenosis. In making this study, one often depended on the past history, as obtained from the patient, for information concerning the type of hemoptysis that had been experienced. Obviously, this approach involves some error. It would appear, however, that the general statements made above concerning the patients who had attacks of acute pulmonary edema were equally true of those who had bouts of hemoptysis.

EMBOLI

It is difficult to obtain exact information as to the total occurrence of emboli in these cases. In most instances we depended on the past history as given by the patient. No doubt, many emboli were overlooked either by the patient or by the attending physician, and some may well have occurred that could not possibly have been recognized. With this limitation it was estimated that 16 different patients had had emboli before the operation, 6 of whom had had more than one embolus, either arterial or pulmonary. There was a total number of 26 emboli among these 16 patients. This is, no doubt, a minimum figure. Ten of these were cerebral, 8 pulmonary, 2 renal, 2 splenic, and 4 in the limbs. Among the 16 patients, 3 had only pulmonary emboli, while the others had arterial emboli. Our main interest was in arterial emboli, since, undoubtedly, these must have arisen from the heart, whereas pulmonary emboli, even in cardiacs, more frequently than not come from venous thrombi in the legs. From a clinical point of view, cerebral emboli are the most important, because they are the most disastrous in their effects. Splenic infarction rarely is of any ultimate consequence; the same is true of renal embolus, except for the rare instance in which hypertension results from unilateral kidney ischemia (Goldblatt mechanism). Embolism to the upper extremity almost never becomes a surgical problem; embolism to the legs, however, not infrequently is a matter of great concern. There are instances in which prompt embolectomy is required in order to prevent gangrene and the loss of a limb.

The most frequent, important, and disabling type of emboli in mitral stenosis is the cerebral. This often occurs in mitral cases at a time when there is comparatively little other disability, when breathlessness is at a minimum and when the patient is fairly active physically and has a sense of well being. In other words, a cerebral embolus causing permanent, partial, or complete paralysis of one side of the body often occurs unexpectedly when the patient is doing well. In contrast, it appears to occur much more rarely during the later years of chronic progressive congestive failure with marked dyspnea, orthopnea, pitting edema, engorged liver, and long-standing auricular fibrillation.

A study of the 16 patients throws light on this relationship. It is of interest that 15 of these had permanent auricular fibrillation, while 1 had repeated transient bouts of this irregularity. This latter case is of particular interest because on several occasions cerebral emboli occurred a day or two after a bout

of auricular fibrillation had ceased. It would appear that emboli are most likely to become dislodged shortly after a thrombus has formed in the left auricle. Furthermore, an embolus is also more likely to occur soon after auricular fibrillation first appears, and can be abruptly dislodged after a previously fibrillating auricle begins contracting normally again. The practical conclusion from the foregoing observations is that anticoagulant therapy might well be employed as a prophylactic measure against embolism, for some days or a few weeks, directly after the onset of auricular fibrillation in cases of mitral stenosis.

In the 8 patients who developed cerebral emboli, the complication occurred within a few days after the onset of auricular fibrillation. In 5 of these the time relationship was quite accurately known, and in the others it was probable. It is remarkable that there was no instance in which a cerebral embolus developed *years* after the onset of permanent auricular fibrillation; this undoubtedly occurs and would be found in a larger series of patients, although it is comparatively uncommon. If this reasoning is correct, it explains the decreasing incidence of cerebral emboli in mitral stenosis in the natural course of the disease during the years following the onset of auricular fibrillation. This decrease needs to be considered when analyzing the occurrence of cerebral emboli during the years following mitral valvuloplasty. Although there has been a sharp, apparent decrease in such cerebral complications during the years following mitral surgery, as compared to the incidence before the operation,[8] the decrease is to some extent more apparent than real, for during those years the incidence of arterial emboli becomes progressively less without surgery.

One might ask what clinical results are to be expected from mitral surgery in the group which previously had had emboli. It would appear from this small series that the immediate operative risk is slightly greater, but that the ultimate improvement in the cardiac status is about the same as that in those patients who had not had emboli previously. Among the 16 patients operated upon who had had emboli, 3 died during or shortly after the operation and 1 died during the follow-up period. The average degree of improvement in the 12 survivors was 2.0, as compared to 2.4 in those who had had no emboli previously. There is, therefore, only a slight difference in the expected improvement from surgery in the two groups. There is the rare possibility of permanent mental impairment after a cerebral embolus. This occurred as a result of surgery in one case in this series. What is of greater importance is that there was no instance of cerebral embolism in any of the patients during the entire follow-up period after they had left the hospital, i.e., 2,436 patient years.

CONGESTIVE FAILURE

It is obvious that those patients who had objective evidence of congestive heart failure were, as a group, sicker than those who did not. Patients who had an engorged liver were almost invariably in Group III or IV severity. The immediate operative mortality was greater in the sicker individuals, but it is of interest that among those who recovered, the degree of improvement was about the same whether they did or did not have objective congestive failure. This does

not mean that the severer cases did as well after the operation as the mild ones; those who were very sick before operation would be regarded as obtaining marked improvement if their condition changed strikingly for the better, although, obviously, they were not as well at their best as were some of the milder cases who had improved on surgery.

ELECTROCARDIOGRAMS

An analysis was made of the electrocardiographic findings obtained a short while prior to surgery. Of 70 patients in whom this information was available, 35 had right ventricular hypertrophy (RVH), 14 showed combined ventricular hypertrophy (CVH); 18 had no ventricular hypertrophy; 1 had left ventricular hypertrophy (LVH); and 2 had electrocardiographic findings within normal limits.* It was of interest to correlate the electrocardiographic findings with the degree of stenosis found by the surgeon during his exploration. In the 35 patients with RVH the average degree of stenosis was 2.9 ("tight" stenosis). In the 18 patients with no electrocardiographic evidence of ventricular hypertrophy, it was calculated to be 2.9, and in the 14 patients with combined ventricular hypertrophy, it was 2.7 ("moderate" to "tight" stenosis). There apparently was a similarity in valve size irrespective of the electrocardiographic findings.

There was likewise a lack of correlation between the electrocardiographic findings and the ultimate clinical improvement. In 24 patients with RVH the average improvement was 2.1 (moderately improved). In the 14 patients with combined ventricular hypertrophy the average improvement was 2.3, and in the 18 patients with no ventricular hypertrophy it was 2.2. It seems, therefore, that there was no difference in improvement between those who had RVH and those who had the additional LVH. Among the patients who were classified as showing no ventricular hypertrophy there could very well have been a number of cases with combined ventricular hypertrophy in which the electrocardiographic signs of either hypertrophy masked the other. So long as the electrocardiograms showed evidence of right ventricular hypertrophy, no matter if LVH was found also, the ultimate result was good. To be sure, the results were satisfactory because these cases included only one that showed preponderant left ventricular hypertrophy. Such cases did not appear in this series because they would not have been regarded as suitable for mitral surgery. They would have shown evidence of too much aortic valvular disease or of mitral insufficiency or other causes of left ventricular hypertrophy.

In the 35 patients with RVH the average systolic blood pressure was 129.4 mm. Hg; in the 14 patients with combined ventricular hypertrophy it was 128.6 mm. Hg; in the 18 patients with no electrocardiographic signs of ventricular hypertrophy it was 129.2 mm. Hg. The blood pressure was obviously the same irrespective of the electrocardiographic evidence of right or left ventricular hypertrophy. In all but 3 of the patients who had a normal sinus rhythm, the electrocardiograms showed a "P" mitrale.

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*Criteria for ventricular hypertrophy in the electrocardiograms are those of S. A. Levine.[15]

X-RAY

Information concerning x-ray examination of the heart before the operation was available in 65 patients of this series. The transverse diameter of the heart and the size of the pulmonary artery were estimated. The former was calculated as percentage increase in the size of the heart as compared to the normal standards determined from the height and weight of the individual. The terms "slight" (up to +15 per cent, "moderate" (15 to 35 per cent), "marked" (35 to 75 per cent), and "extreme enlargement" (over +75 per cent) were used. Similar terminology was employed in designating the enlargement of the pulmonary artery.

The average enlargement of the transverse diameter of the heart in the 65 patients was 28.1 per cent. For the 10 patients in Group 1 (slight enlargement) the clinical postoperative result was 2.4. For the 29 patients in Group 2 (moderate enlargement) the result was 2.3, and for the 14 patients in Groups 3 and 4 it was 2.1. The average blood pressure in these groups was about the same. It is evident that the clinical improvement to be expected from mitral surgery varied only very slightly in favor of those patients with a smaller heart. This was true in these cases because of the proper selection of patients. In general, the larger the heart the poorer the prognosis. Many patients with very large hearts, who would very likely do poorly, had already been eliminated because they obviously had primary mitral insufficiency or an accompanying aortic insufficiency, or some other factor that would militate against obtaining a satisfactory result from mitral surgery.

The average enlargement of the heart among 25 patients who had a past history of acute pulmonary edema was +25.6 per cent, as compared to +29.5 per cent in the remainder. The former seemed to have a slightly smaller heart. It is also of interest, and not surprising, that the larger hearts had a louder systolic murmur than the smaller, the averages being a grade of 1.7 for Groups 3 and 4 enlargement and a grade of 0.8 for the Groups 1 and 2 enlargement.

The average enlargement of the pulmonary artery was designated as 1.9 (moderate). The size in the 9 patients with a "very tight" mitral stenosis was 2.3, while the size in the 10 patients with a "moderately tight" stenosis was 1.7. This would indicate quite clearly that the larger pulmonary arteries were associated with a higher degree of mitral stenosis. On the contrary, the pulmonary artery tended to be slightly smaller in those patients with a past history of acute pulmonary edema than in those without such a history. The average size in 24 patients with a history of acute pulmonary edema was 1.7, while the figure for the other 43 patients was 2.0.

A comparison was made between the size of the mitral valve as estimated by the surgeon at the time of the operation and the x-ray size of the heart. In 8 patients with "very tight" valves the average heart size was +28.4 per cent, for 43 patients with "tight" valves it was +29.2 per cent, for 10 patients with "moderately tight" valves it was +20.2 per cent, and for the 3 patients with predominant mitral insufficiency and minor stenosis it was +67 per cent. Although it is well known that those with predominant mitral insufficiency have

very large hearts, it was of interest that those with only moderate stenosis should have smaller hearts than those with very tight stenosis.

AGE FACTOR: OVER AND UNDER 50 YEARS

The physician may be reluctant to advise mitral operations in elderly patients. It was of interest, therefore, to compare some of the preoperative clinical features, such as the valve size found at operation and the clinical result achieved, in patients who were over 50 years of age with those in patients who were under 50 years of age at the time of the operation. Out of a total of 71 patients, 9 were over, and 62 were under, 50 years of age.

The average blood pressure in those over 50 years old was 143/89 mm. Hg; and in the younger age group it was 127/82 mm. Hg. In the older age group, 4 of the 9 had objective evidence of congestive heart failure. In the younger group, 24 out of 62 had objective evidence of congestive heart failure. In the older group, 8 out of 9 had auricular fibrillation, while in the younger group, 38 out of 62 had auricular fibrillation.

The electrocardiograms of the 9 older patients showed right ventricular hypertrophy in 6, combined ventricular hypertrophy in none, no ventricular hypertrophy in 2, and isolated left ventricular hypertrophy in 1. Among the 61 patients under 50 years of age there were 29 with right ventricular hypertrophy, 14 with combined ventricular hypertrophy, 17 with no ventricular hypertrophy, and 1 with a normal electrocardiogram.

The degree of stenosis found by the surgeon during the operation in the two age groups was as follows: among the 9 patients over 50 years, "very tight" stenosis was found in none, "tight" stenosis in 8, "moderately tight" stenosis in 1, and in no case was the valve found to be mainly regurgitant. The average degree of stenosis for this group was 2.9. Among the 62 patients of the younger age group, a "very tight" mitral stenosis was found in 11, a "tight" stenosis in 35, a "moderately tight" stenosis in 10, and only minor stenosis in 4. The average degree of stenosis in this group was 2.8. Of the 9 older patients, 2 died during or immediately after the operation; the average degree of improvement in the 7 survivors was 1.3. Of the 62 patients in the younger group, 4 died at or immediately following the operation. The average degree of improvement among the survivors was 2.3. From this analysis it seems that the only difference in the preoperative status of the two groups was the older group's higher average blood pressure (probably a late development in the natural history of the disease), higher incidence of auricular fibrillation (again a consequence of the longer duration of their mitral disease), and slightly greater general clinical disability. The degree of stenosis found at operation did not differ significantly in the two groups, except that "very tight" stenosis was not present in the 9 older patients. The operative mortality was probably higher in the older age group, and the degree of benefit obtained from the operation seems to have been less in the older than in the younger group.

Another analysis of the age factor in these cases was made. The average age of those 7 patients who improved the most (grade 4) was 36.7 years; for the

24 with grade 3 improvement it was 41.4 years; and for the 12 with grade 2 improvement it was 44.3 years. There was, therefore, a steady increase in the average age as the results from surgery worsened. Although the older patients did not do quite so well as the younger ones, it does not follow that age per se was the cause of the deterioration of their chances. The older patient may well have had slightly more congestive failure, or slightly larger hearts, or poorer coronary arteries. It is evident that age is only a slight factor, for satisfactory results are frequent in patients over 50 years of age.

PREOPERATIVE DEGREE OF STENOSIS (VALVE SIZE) AND POSTOPERATIVE CLINICAL RESULTS

The primary aim of mitral valvuloplasty is to relieve the obstruction to the diastolic filling of the left ventricle produced by a stenosed mitral valve. The more stenosed, the greater will be the relative relief by successful surgery and, therefore, the better the clinical result. It is obvious that many other factors, favorable and unfavorable, such as sex, age, presence or absence of other valvular lesions, will influence the ultimate outcome. Nevertheless, if it is correct that the main benefit from mitral surgery is the consequence of a mechanical relief of stenosis, then a correlation between preoperative valve size and postoperative improvement should be found. This proved to be so in this series of cases.

In 9 patients in whom the surgeon found a mitral valve to be "very tightly" stenosed, the average postoperative improvement was 3.3 (marked to excellent improvement); in 34 patients in whom the valve at operation was considered as "tight" stenosis, the average postoperative improvement was 2.4. In the 12 patients with a "moderately tight" stenosis, the improvement averaged 1.2, and finally in the 4 patients in whom at operation mitral regurgitation was found to be predominant and mitral stenosis only slight, the average improvement was calculated at 0.

It follows that the tighter the stenosis, the better the result that can be expected. Therefore, preoperative estimation of the tightness of the stenosis will be a most important factor to be assessed when mitral surgery is comtemplated. The preoperative degree of clinical severity of these four groups of cases of mitral stenosis was much the same, i.e., 2.6 for the "very tight" and 3.0 for the other three groups. It follows that the tightest cases did best not because they were milder or more severe to begin with, but because they were mechanically more stenosed.

The Surgeon's Estimate of Expected Operative Success.—It was of interest to compare the impression that the surgeon had at the time of the operation as to how complete a valvuloplasty he achieved, with the actual clinical result observed in these patients during the follow-up period. The surgeon's impression of the completeness of the operation was judged in the following manner, according to his own description in the operative protocol: What the surgeon considered to be a "fair" result was called grade 1; a "good" result, grade 2; a "very good" result, grade 3; and an "excellent" valvuloplasty, grade 4.

Of the 4 patients whom the surgeon considered to have had a "fair" valvulo-

plasty 1 died shortly following the operation; and in the 3 survivors the average clinical result was calculated to be 0. Of the 11 patients who were thought to have had a "good" valvuloplasty, 1 died following the operation, and the average clinical result of the 10 survivors was 2.6, i.e., moderate to marked improvement. Of the 22 patients who were thought to have had a "very good" valvuloplasty 2 died in the postoperative period, and in the 20 survivors the average clinical result was 2.5, i.e., moderate to marked improvement. Of the 17 patients who were considered by the surgeon to have had an "excellent" valvuloplasty none died in the postoperative period, and the average clinical improvement was 2.8.

It seems from the foregoing that the surgeon predicted fairly well when the result was not going to be satisfactory. However, in the others he could not foretell whether the degree of improvement would be only moderate or very great. It must be appreciated that when the surgeon estimates the size of the mitral valve to be 3 or 4 cm., after the operation, he does so by pushing his fingers through the valve. It is very doubtful that the valves open as readily or to as wide a degree when the leaflets move merely as a result of differences of pressure in the left auricle and ventricle. The force of the fingers is likely to be much greater than that of auricular systole or pressure. Furthermore, it is idle for the surgeon to maintain after an operation that "there is no longer any mitral stenosis," for the very signs on which the original diagnosis of mitral stenosis was correctly made persist after "excellent" repair of the valve is accomplished. Undoubtedly, the constriction of the valve is lessened, but it is rarely if ever entirely relieved.

DISCUSSION

Although in the large majority of cases the diagnosis of mitral stenosis can be made quite readily from simple auscultation, there are some, mainly those that show no apical diastolic or presystolic murmur whatsoever, in which the diagnosis may be quite difficult. There are then many clues and combinations of findings that form the basis on which the diagnosis will have to rest. Most of these points individually are not diagnostic; the final decision, therefore, will have to rest on the judgement and experience of the observer. The most important of the clues is the detection of a calcified mitral valve on fluoroscopic examination. This is practically pathognomonic when it can be differentiated from a calcified mitral annulus, for the latter is generally accompanied by no mitral stenosis. Other clinical features supporting the diagnosis of mitral stenosis are: an opening snap, accentuated first sound, accentuated and reduplicated pulmonary second sound, enlarged left atrium, pulmonary artery or right ventricle on x-ray examination, right ventricular hypertrophy or P-mitrale in the electrocardiograms, past history of rheumatic fever, auricular fibrillation, increased $Q\text{-}M_1$ interval and short $S_2\text{-}OS$ interval.* This evidence can be obtained either by simple auscultation or by the use of apparatus that is readily available.

*The $Q\text{-}M_1$ interval is the time between the Q wave in the electrocardiogram and the first heart sound in the phonocardiogram. The $S_2\text{-}OS$ interval is the time between the second heart sound and the opening snap.

Yet, there will remain instances in which the diagnosis will be obscure. Catheterization studies of the left and the right side of the heart may become necessary in order to determine either the presence or the degree of mitral stenosis. Even such studies can leave one in doubt. The finding of an increased "wedge pressure," or better still an appreciable gradient in the diastolic pressure between the left atrium and the left ventricle, will help in the diagnosis. Finally, angiocardiographic visualization of the chambers of the heart, when expertly carried out, may be diagnostic.

It becomes clear from this study that in most cases a definite diagnosis of mitral stenosis can be made with the expectation of finding sufficient constriction of the valve to make surgery worth while. There will also be a group in which the diagnosis of primary mitral insufficiency will be made, but in which no significant stenosis will be present. In such cases surgery will be indicated only if the operative approach to mitral insufficiency becomes a satisfactory procedure. These latter cases will often show very large hearts with huge left auricles, left ventricular hypertrophy, and other evidence of mitral valvular disease, even including the diastolic murmur and thrill of the type seen in well-marked mitral stenosis. However, there will remain a small group in which the exact degree of mitral stenosis will be uncertain. There will be no doubt that the mitral valve is diseased, but the relative degree of insufficiency and constriction of the valve will be puzzling. It is not at present certain whether left heart catheterization or angiocardiography will be sufficiently worth while diagnostically to warrant the discomfort and the slight risk involved in these procedures. In such cases an exploratory operation of the heart might well be indicated, just as similar exploratory operations are performed in other parts of the body when diagnosis is difficult.

A review of the operative results obtained in the 71 mitral cases in this study adds further evidence that surgery can now be carried out with a reasonably low risk and with the expectation of considerable improvement in the health of most patients. We also feel that the improvement that is obtained can be ascribed, for the most part, to the actual operation and not to better medical care or to psychologic factors. This does not preclude the latter from playing a definite, but minor, role in some cases.

In the selection of cases an accurate diagnosis of mitral valvular disease is of first importance. Secondly, one would like to be sure that sufficient valvular stenosis will be found, i.e., a valve less than 1.5 sq. cm., and preferably less than 1.0 sq. cm. In some cases with only slight or moderate stenosis and a history of arterial emboli, the operation might yet serve a useful purpose in diminishing the future likelihood of disabling peripheral emboli. This beneficial result might follow the simple amputation of the auricular appendage, whenever the latter contains the only site of mural thrombosis. At present one would prefer to choose those mitral cases that have little if any additional valvular disease. However, the presence of aortic or tricuspid disease by no means prohibits surgery. There are many instances in which it is evident that although other valvular defects are present, the stenosed mitral valve is mainly responsible for the symptoms.

In other cases the surgeon will be able to operate on the aortic valve at the same time as on the mitral valve. In fact, there have been rare instances (not carried out in this series) when the surgeon was daring enough to attack the mitral, aortic, and tricuspid valves during the same operation.

There are other factors to be considered in the selection of cases. One obviously would delay operation if the patient were suffering from bacterial endocarditis. The same is true if active rheumatic fever or active rheumatic carditis were present. There are times, however, when it is difficult or impossible to be sure about the presence of a smouldering rheumatic state. One would prefer to await the disappearance of fever, leukocytosis, increased sedimentation rate, and other signs that point to continued infection. Whenever any of these features were present, we still permitted operation if the patient felt fairly well, was eating satisfactorily, and appeared to be in a status quo. There were instances in which operation was performed with gratifying results while a temperature of 100 to 101° F. was still continuing. Such apparently ill-advised hastiness was resorted to because of economic reasons and, partly, because it seemed that more was to be gained by operation than by further prolonged waiting. These are difficult decisions, for our views as to the meaning of "rheumatic activity," the significance of Aschoff nodules, and the clinical importance to be placed on this or that sign are all quite vague. The general appearance of the patient probably remains as good a guide as any.

One would hesitate to select a patient who has obvious coronary artery disease, especially if it appears that on that basis alone the outlook is not promising. Not only would the immediate risk from surgery be great, but the postoperative life expectancy would probably to too short to warrant the risk. Whereas several years ago patients over 50 year of age were regarded as too old, the operative mortality since then has so decreased that now even cases over 60 years of age are occasionally regarded as suitable for surgery.

Major cardiac surgery is still much too risky to recommend as a purely prophylactic procedure in patients with well-compensated mitral stenosis. There are many such patients who live an essentially normal life for a great many years. A women's champion long-distance swimmer was found to have classical mitral stenosis, but she could swim 20 miles without difficulty. One of us has been following a patient who has had definite mitral stenosis of 38 years' duration. This patient is now about 55 years old and is leading a normal life. Another patient, a school janitor, showed definite evidence of mitral stenosis and auricular fibrillation at the age of 50 years. Twenty-one years later he was still well and working, climbing stairs, had no signs of congestive failure, and showed the same evidence of mitral stenosis, auricular fibrillation, and a slow ventricular rate. Although most cases do not progress so favorably as these, it would have been unwise to subject such individuals to what would have proved to be an unnecessary surgical operation.

A logical inference from the foregoing is that obvious evidence of downward progress is one of the best criteria for the selection of patients for mitral surgery. On following a patient who is doing well or well enough, is able to work and enjoy moderate things in life, and is not losing ground, one would be justified in continu-

ing a conservative course of so-called medical management. When and if definite evidence appears that ground is being lost, when there is increasing dyspnea, the vital capacity of the lungs is diminishing, or other clinical clues appear that indicate a loss of cardiac reserve, surgery becomes indicated. In other words, one is justified in letting well enough alone when the situation is satisfactory and compatible with the enjoyment of a useful life, but surgical intervention is desirable when deterioration sets in. The exact point at which drastic action is advisable is often an individual matter, depending on many factors, medical, economic, and social, and at times will be judged differently by various competent physicians.

SUMMARY

Seventy-two patients subjected to mitral valvuloplasty were studied. They were all personally examined before and after operation. An analysis was made of the clinical features that might serve as a guide to the severity of the condition, the risk of the operation, and the degree of improvement to be expected.

There were 61 females and 11 males (ranging in age from 27 to 62 years). The average age at the time of the operation was 44 years. There were 6 surgical deaths, 1 in the operating room and 5 during the immediate postoperative days. During more recent years the operative mortality in Group III cases has fallen to about 1 per cent. There were 5 fatalities during the follow-up period, with an average survival of 36 months. The average follow-up period of the living patients was 42 months. The patients were divided preoperatively into four groups: Group I (symptomless), no patients; Group II (slight limitation), 19 patients; Group III (significant symptoms on slight effort), 41 patients; Group IV (seriously ill with irreversible failure), 11 patients. The average disability of the entire group was 2.9. The figures were 3.2 for those who died during the operation and 3.3 for those who died during the follow-up period.

The postoperative clinical results were designated as: worse, unchanged, improvement (1) slight, (2) moderate, (3) good, and (4) excellent. Among the 58 patients who survived, and for whom results were known, 3 were worse, 5 were unchanged, and 7 had grade 1 improvement, 12 grade 2, 24 grade 3, and 7 grade 4.

The degree of postoperative improvement declined somewhat with increasing blood pressure. The degree of stenosis was less among the hypertensive patients. In fact, no hypertensive patient had a "very tight" stenosis.

Although a murmur in diastole at the apex is the most useful diagnostic sign of mitral stenosis, its intensity is only a fair guide to the degree of stenosis. Very tight stenosis was found with faint diastolic murmurs, and very slight stenosis with loud ones. Although the louder apical systolic murmurs generally signified more mitral regurgitation and a less favorable result from surgery, there were 6 exceptions. In these 6 cases, although the apical systolic murmur was loud or louder than the diastolic, there was a high degree of mitral stenosis. In the selection of patients for surgery, basal murmurs can be dismissed, for the

most part, if there is electrocardiographic evidence of right ventricular hypertrophy.

An accentuated apical first sound was found to be fairly good evidence of mitral stenosis but was also present with predominant mitral regurgitation.

When the mitral valve was found to be calcified, the average intensity of the first heart sound was less, and the immediate risk of operation slightly greater, and the ultimate result was not quite so good as when the valve was not calcified.

Those patients who had attacks of acute pulmonary edema or hemoptysis, or both, comprised a fairly distinct group. They generally showed a normal sinus rhythm, did not have great cardiac enlargement, had little if any evidence of right heart failure, and did very well both during the operation and in the follow-up period.

Among 71 patients, 46 had auricular fibrillation at the time of operation. Of the 25 with a normal sinus rhythm, 8 developed auricular fibrillation during or shortly after the operation. It did not appear worth while to try regularization with quinidine before the operation or to use it after the operation in those who had had persistent fibrillation. Quinidine was helpful in some who developed the arrhythmia during or after the operation.

The occurrence of previous arterial emboli made the operative risk slightly greater and the ultimate result slightly less favorable. However, operation appeared to lessen the likelihood of future cerebral emboli. Of the 16 patients who had previous emboli, 15 had chronic auricular fibrillation, while 1 had only transient bouts of the arrhythmia. None developed cerebral emboli during the follow-up period.

The presence or absence of right ventricular hypertrophy in the electrocardiograms did not aid in predicting how tight the mitral valve would be nor how well the patient would do postoperatively. However, the clinical results were good if the tracing showed right ventricular hypertrophy, even if left ventricular hypertrophy was also present. The presence of left ventricular hypertrophy alone would militate against an expected favorable operative result.

The average increase in the transverse diameter of the heart on x-ray examination was 28.1 per cent. The degree of improvement was not much different in those with greater enlargement than in those with less enlargement, although the larger hearts were found in those who were more gravely ill. Patients with huge hearts such as are seen with mitral insufficiency were, for the most part, not selected for surgery. Those with "very tight" mitral stenosis had larger hearts (+28.4 per cent) than those with "moderately tight" valves (+20.2 per cent). The size of the pulmonary artery was greater in those with "very tight" than in those with "moderately tight" valves.

An analysis of the age factor indicated that older patients did not do quite so well as the younger patients. Factors other than age, however, such as greater frequency of congestion, auricular fibrillation, or cardiac enlargement and the complete absence of "very tight" valves in the older group, must play a role.

A comparison of the valve size as found at operation and the postoperative clinical result clearly indicates that those with the tightest valves do best.

The surgeon's prediction as to how much improvement would take place by the type of valvuloplasty he accomplished was only partly accurate. When he thought the operation was "excellent," the results were the best, and when he thought it was only "fair," the results were poor. However, when he thought it was "good" or "very good," the results varied and were about the same in the two groups.

At the present stage of mitral valve surgery, the physician's goal is to select those cases that have the minimum degree of insufficiency and the greater degree of stenosis. The present experience affords convincing evidence that the mechanical factor of valvular defect is most important in causing the disability from rheumatic heart disease, a view that was belittled a few decades ago.

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REFERENCES

1. Cutler, E. C., and Levine, S. A.: Boston M. & S. J. **188**:1023, 1923.
2. Souttar, H. S.: Brit. M. J. **2**:603, 1925.
3. Harken, D. E., Ellis, L. B., Ware, P. F., and Noonan, L. R.: New England J. Med. **239**:801, 1948.
4. Harken, D. E., Ellis, L. B., and Noonan, L. R.: J. Thoracic Surg. **19**:1, 1950.
5. Bailey, C. P.: Dis. Chest **15**:377, 1949.
6. Lewis, Sir Thomas: Diseases of the Heart, New York, 1937, The Macmillan Co., p. 144.
7. Levine, S. A.: The Great Importance of Valvular Injury in Rheumatic Heart Disease, Libro Homenaje al Profesor Doctor Ignacio Chavez, p. 185. Editads por la Universidad Nacional Automonia México, 1945.
8. Ellis, L. B., and Harken, D. E.: Circulation **2**:637, 1955.
9. Wood, P.: Brit. M. J. **1**:1051, 1113, 1954.
10. Likoff, W., and Uricchio, J. F.: J.A.M.A. **166**:737, 1958.
11. Levine, S. A., and Fulton, M. N.: Am. J. M. Sc. **186**:465, 1928.
12. Freeman, A. R., and Levine, S. A.: Ann. Int. Med. **6**:1371, 1933.
13. Schilder, D. P., and Harvey, W. P.: Am. Heart J. **54**:352, 1957.
14. Gorlin, R., Lewis, B., Haynes, F. W., and Dexter, L.: Am. Heart J. **43**:357, 1952.
15. Levine, S. A.: Clinical Heart Disease, Ed. 5, Philadelphia, 1958, W. B. Saunders Company, pp. 435-456.

The Electrocardiogram in Scleroderma: Analysis of 60 Cases and Review of the Literature

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Since the paper of Weiss and associates[1] reporting 9 cases of scleroderma heart disease, other authors have described new cases, making mention of the electrocardiographic changes found in such patients. However, most of these reports concern a small number of cases, and the electrocardiograms are not discussed in detail.† Several electrocardiographic alterations have been described, all of them nonspecific.

The purpose of this article is to report our experience with a larger series of patients, correlating the electrocardiograms with the clinical, physiopathologic, and morphologic findings.

MATERIAL AND METHODS

The charts of 60 patients with scleroderma were selected from the files of the New York Hospital, and divided into two groups.

Group I included 31 patients with typical scleroderma of the skin, *without* clinical or radiologic manifestations of visceral involvement. They included 23 white females and 8 white males, ranging in age from 14 to 68 years (mean 36 years). The development of the disease in these cases covered periods of between 1 month and 20 years (mean 6 years).

Group II was composed of 29 patients with typical scleroderma of the skin, *with* visceral involvement, either heart, lungs, kidneys, or esophagus. There were 23 white females and 6 white males, ranging in age from 27 to 73 years (mean 50.6 years). The duration of the disease in these cases ranged between 3 months and 27 years (mean 5.5 years). Seven of the 29 patients died and autopsy was performed.

Patients with other diseases complicating scleroderma were not included in either group. Other factors with possible influence on the electrocardiogram were also taken into account, such as anemia, metabolic disturbances, or certain medication, especially digitalis. One or more electrocardiograms from each patient were studied for the determination of the rhythm, heart rate, P-R, QRS, and Q-T intervals, as well as for calculation of ÂQRS, ÂP, and ÂT in the frontal plane.

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†After this paper was prepared, a new report by Windesheim and Parkin appeared.[22]

RESULTS

In Group I (*without* apparent visceral involvement) the electrocardiogram was within normal limits in 23 of the 31 patients (74.2 per cent). Twelve of these 23 had isolated electrocardiographic alterations such as notching of the P wave or slurring of QRS on standard leads. However, in 8 patients (25.8 per cent) the electrocardiogram was definitely abnormal.

TABLE I. ELECTROCARDIOGRAPHIC RESULTS

			GROUP I		GROUP II	
			CASES	PERCENTAGE	CASES	PERCENTAGE
Rhythm	Normal sinus		31	100	27	93.1
	Nodal. Wandering pacemaker and sinus arrest		—	——	1	3.4
	Idioventricular. Complete A-V block		—	——	1	3.4
Extrasystoles	Ventricular		1	3.2	1	3.4
	Nodal		—	——	2	6.9
	Multifocal (on digitalis)		—	——	1	3.4
	Short run of paroxysmal auricular tachycardia		—	——	1	3.4
Prolonged (0.06 sec.) Q-T-MV*			—	——	1	3.4
Notching of P wave on standard leads			14	45.2	17	60.8
Slurring of QRS. No BBB			4	12.9	3	10.3
Low voltage			4	12.9	8	27.6
Incomplete bundle branch block		Right	1	3.2	6	20.7
		Left	2	6.4	2	6.9
Ventricular hypertrophy		Right	1	3.2	2	6.9
		Left	1	3.2	10	34.5
Auricular enlargement		Right	—	——	1	3.4
		Left	—	——	1	3.4
Ischemia	Subepicardial		—	——	5	17.2
	Subendocardial (or subepicardial hyperemia ?)		—	——	1	3.4
Injury	Subepicardial		—	——	—	——
	Subendocardial		—	——	2	6.9

*Value of the Q-T interval in relationship with the Mean Value, in accordance with the Bazett's formula: $Q\text{-}T = 0.39 \sqrt{R-R}$.

TABLE II. FINDINGS IN THE SEVEN AUTOPSIED CASES

CASE	AGE (YR.)	SEX	TIME OF EVOLUTION	ELECTROCARDIOGRAM	AUTOPSY
1. E.M. (H.R.: 628894)	60	M	2 yr. Heart failure: 3 mo.	Nodal extrasystoles. Low voltage. Nonspecific auricular, ventricular, and perinodal alterations	Scleroderma. Pericardial effusion (1,000 c.c.). Pleural effusion. Interstitial myocardial fibrosis. Numerous linear accumulations of collagenous tissue in the left auricle and ventricle. Kidneys: proliferation of the medium-sized vessels. Several small infarcts
2. W.C. (H.R.: 611275)	64	M	3½ yr.	IRBBB. Shift of ÂP and ÂQRS to the right in 3 yr. Auricular myocardial alterations	Scleroderma. Pulmonary fibrosis. Cardiomegaly. Slight myocardial fibrosis involving also the I-V septum. Endocardial thickening in the left auricle. Coronaries patent
3. I.S. (H.R.: 564888)	56	F	Raynaud's phenomenon since childhood. General symptoms: 1 yr.	L.V.H. Low voltage. Diffuse disturbance of the ventricular repolarization. Subepicardial ischemia. Auricular myocardial alterations	Scleroderma. L.V.H. Considerable interstitial myocardial fibrosis. Diffuse infiltration by polys in the anterior epicardium. Coronaries patent. No pericardial effusion. Kidneys: advanced proliferative endarteritis. Numerous infarcts
4. J.H. (H.R.: 659899)	62	M	7 mo.	ILBBB of first degree. Auricular myocardial alterations	Scleroderma. Myocardial fibrosis. Intimal thickening of small arteries. Coronaries patent. Kidneys: interstitial fibrosis in some smaller arteries. Lungs: slight fibrosis
5. H.F. (H.R.: 528866)	53	F	15 yr.	Abnormal ventricular repolarization: subendocardial ischemia or subepicardial hyperemia? Auricular myocardial alterations	Scleroderma. Fibrinous pericarditis, most marked over right auricle. L.V.H. Subendocardial petechial hemorrhage. Thickening of the mitral valve. Kidneys: fibrosis of small arteries. Acute necrotizing panarteritis and arteriolitis (?) with infarcts. Lungs: slight fibrosis
6. M.S. (H.R.: 738532)	56	F	5½ yr. Heart failure: 2 yr.	Wandering pacemaker. IRBBB. Right auricular enlargement (qR on Leads V_1, V_2). R.V.H. Anterior subendocardial lesion. Severe digitalis toxicity. Compatible with cor pulmonale	Scleroderma. Cardiomegaly, especially right chambers. Subendocardial ischemia. Coronaries patent. Lungs: fibrinous thickening of bronchovascular walls. Chronic cor pulmonale
7. R.E. (H.R.: 442800)	55	M	4 mo.	Complete A-V block with idioventricular rhythm. Auricular and ventricular disturbances	Scleroderma. Calcification of the membranous interventricular septum. Fibrosis and disruption of the bundle of His. Sclerosis of small and medium arteries. Coronaries patent. Lungs: fibrosis and silicosis

In Group II (*with* visceral involvement by the disease) the electrocardiogram was abnormal in 22 of the 29 patients (75.9 per cent). The remaining 7 (24.1 per cent) had electrocardiograms within normal limits, although one of these had clinical and radiologic manifestations of heart involvement. On the other hand, 2 patients without clinical diagnosis of heart disease, presented abnormal electrocardiograms; one had incomplete right bundle branch block and subepicardial ischemia, and the other had evidence of left ventricular hypertrophy. Complete results are shown in Tables I and II.

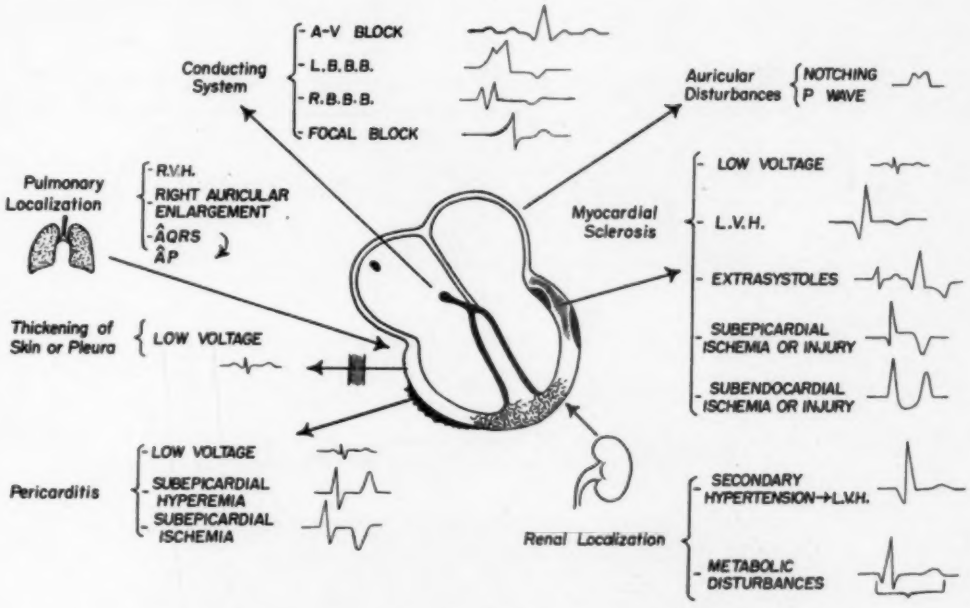

Fig. 1.—Schema showing the theoretical possibilities which may act on the ECG in case of systemic scleroderma.

DISCUSSION

Scleroderma can produce electrocardiographic alterations through the following four major mechanisms: the heart involvement, the pulmonary pathologic changes, the disturbances of the conducting medium, and the renal involvement by the disease (Fig. 1).

1. *The Heart Involvement.*—Scleroderma can affect all structures of the heart, but the one which is more frequently and severely involved is the myocardium. Several findings have been described by pathologists: foci of fibrosis between apparently normal fibers, proliferation of the connective tissue with increased vascularization, or replacement of the normal muscular fibers, wide zones of fibrosis, occasionally transmural, from endocardium to epicardium. In the latter case the great reduction of functioning muscular units may produce a progressive *diminution of the tracing voltage* in directly proportional relationship to the amount of fibrosis. Actually, this has been the cause of low voltage in most of the cases reported in the literature.[2-6] This alteration was present in 12 of our 60 cases (20 per cent), 10 of them related to the myocardial damage alone.

In addition, it has been reported that there is some tendency of the *electrical axis of QRS* (*ÂQRS*) to shift to the left, in the manner frequently seen among patients with arteriosclerotic heart disease. In our series, only 2 patients of Group II with heart involvement alone had an ÂQRS situated to the left of 0°, and the total group failed to show significant deviation (Fig. 2). It is not rare

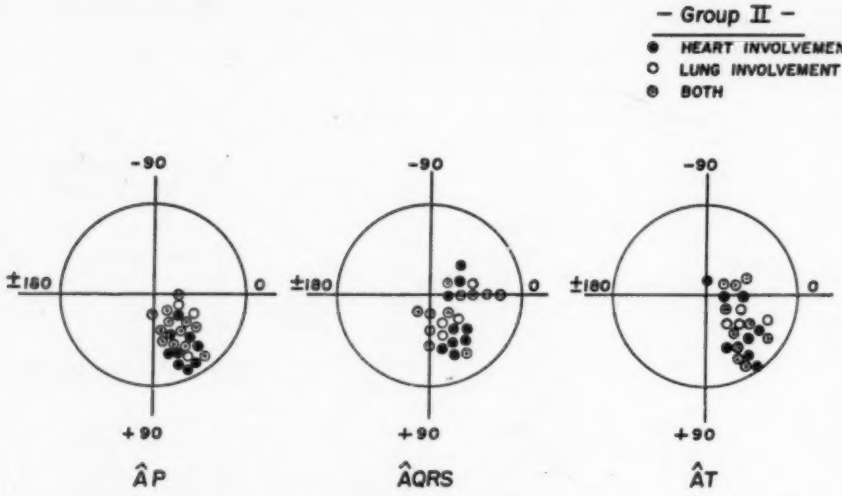

Fig. 2.—Situation of the electrical axis on the frontal plane in cases of heart or lung involvement, or both. There is no characteristic distribution.

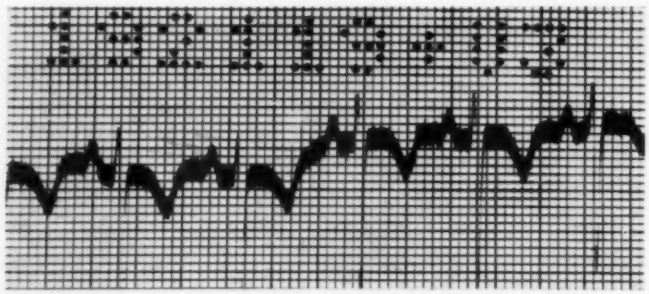

Fig. 3.—G. L. (H. R.: 666929). Lead V_3. Note the deep, symmetrical, negative T waves, due to anteroseptal subepicardial ischemia.

to find changes in the ventricular repolarization suggestive of injury or ischemia. *Subepicardial ischemia*, as evidenced by negative, symmetric T waves, has the highest incidence among the cases previously reported.[1,2,7] Our findings agree with these reports. Evidence of such disturbance was present in 5 patients (17.2 per cent), all of them in Group II (Fig. 3). In one of these there was also evidence of a depolarized zone, without clinical evidence of myocardial infarction; unfortunately, this patient died at home and no autopsy was performed. Because of the lack of evidence of pericarditis in all these patients, and because of the patency of the coronary arteries in scleroderma, it is logical to attribute such subepicardial ischemia to the myocardial fibrosis per se, to the thick-walled arterioles, or to their narrowed lumen.[8]

Subendocardial ischemia is rarely seen in scleroderma, despite the fact that theoretically there is early fibrosis located in the endocardium, with an intramyocardial pressure gradient.[6] In one of our patients the diagnosis of either subendocardial ischemia or *subepicardial hyperemia*[9] was suspected because of the tall and peaked T waves on Leads D_2, D_3, and precordial leads. At necropsy, however, there were pathologic alterations in both the subepicardial and subendocardial areas. Fibrinous pericarditis as well as subendocardial petechial hemorrhages were found. Therefore, a definite explanation of the electrocardiographic findings could not be made.

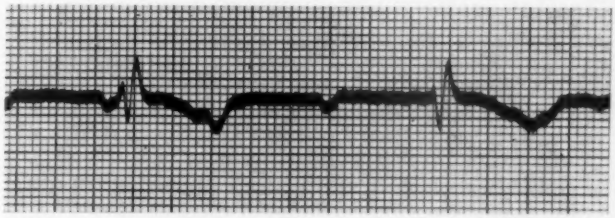

Fig. 4.

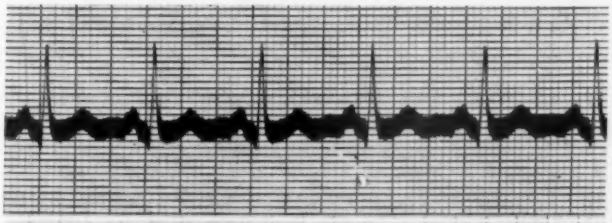

Fig. 5.

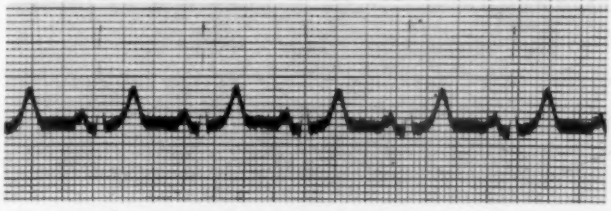

Fig. 6.

Fig. 4.—R. E. (H. R.: 442800). Lead D_3. Complete A-V block with idioventricular rhythm; auricular rate 110, ventricular rate 37.

Fig. 5.—Ch. B. (H. R.: 461347). Lead D_2. Note the notching of the P waves. Interval between peaks is 0.038 second.

Fig. 6.—L. A. (H. R.: 7849). Lead D_2. Another case showing notched P waves. Peak interval is 0.04 second.

Subendocardial lesions (concave RS-T with downward deviation) are not infrequently seen in this disease,[4] but in most instances they appear when digitalis has been administered. Such changes were present in 2 of our cases, both with digitalis toxicity.

Subepicardial lesions (convex RS-T with upward deviation) were not present in any case.

The electrical systole is sometimes altered, and there are a few reports of cases where the Q-T interval was slightly prolonged.[10,11] Only one patient in this series with subepicardial ischemia exhibited prolongation of Q-T.

The presence of various types of *extrasystoles* may occur in scleroderma when the patient is not receiving digitalis, and appears to be due to the myocardial impairment. We found this increase in the automatism of the heart in only 5 patients without digitalis; 2 had ventricular premature contractions, 2 nodal, and the other presented a short run of auricular paroxysmal tachycardia. Extrasystoles were also present in another patient who had been taking the drug. *Auricular fibrillation* was not present in any case, although it has been described by other authors.[1,2,6,11,12] A frequent finding in scleroderma of the heart is a *disturbance of the specific conducting system. A-V blocks* of first degree,[1,8,10,13] occasionally progressive,[10] or complete A-V block with idioventricular rhythm[14] may be present. This latter disturbance was observed in a very interesting patient in Group II, who presented Stokes-Adams episodes, and who died suddenly. The autopsy showed extensive calcification of the membranous interventricular septum, with disruption and fibrosis of the bundle of His (Fig. 4).

*Bundle branch block** is often seen, either right [3,4,15] or left.[1,7,10,13] In our experience, incomplete right bundle branch block was almost twice as frequent as incomplete left bundle branch block and its incidence was higher among those patients in Group II (20.7 per cent as compared to 3.2 per cent in Group I). The incidence of incomplete left bundle branch block was almost identical in both groups (6.4 per cent in Group I; 6.9 per cent in Group II). In Group I it was present in 2 patients. The first was a 46-year-old woman with a 10-year history of the disease. This patient was the same one who presented the ventricular extrasystoles. The other was a 43-year-old woman with a history of scleroderma of 5 years' duration. Complete right or left bundle branch block was present in no instance. *A focal peripheral block*[6] could explain some nonspecific alterations of the QRS complex, such as slurring or notching. These abnormalities we found in 11.7 per cent of all patients, with a similar incidence in both groups.

Myocardial fibrosis is often associated with *ventricular hypertrophy*,† especially left ventricular hypertrophy such as that found in patients with arteriosclerotic heart disease. Weinberg and associates[6] found left ventricular strain in 23.1 per cent of their series. It was present in 10 patients in our Group II (34.5 per cent) and in 1 patient in Group I (3.2 per cent). Of the 10 in Group II, only 3 had hypertension, possibly secondary to renal involvement in some instances. In the remaining 7 patients the left ventricular hypertrophy seems to have been due to fibrosis alone. Three other patients with high blood pressure did not show electrocardiographic evidence of left ventricular hypertrophy. The only patient

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**The criteria used for the diagnosis were: *IRBBB*: "rsr" complex on Lead V_1, with length of QRS < 0.11-0.12 sec., whether such morphology was due to "false" or real block. Other findings, if present, were also taken into account, such as slurring of S on Lead D_1, ÂQRS deviated to the right, or secondary changes of ST-T. *ILBBB*: initial slurring of R wave on Leads D_1-V_5-V_6. Absence of Q wave on the same leads. R wave small or absent on Lead V_1. Length of QRS < 0.11-0.12 sec. Also considered were deviation of ÂQRS to the left and secondary changes of ST-T.

†Criteria for *LVH* were: left ÂQRS deviation, high voltage of QRS, deep S on Leads V_1-V_2, tall R on Leads V_5-V_6. Also considered, if present, were: QRS > 0.12 sec., $(R_1 + S_3) - (S_1 + R_3) > +17$, intrinsicoid deflection > 0.045 sec. on Leads V_5-V_6, secondary changes of ST-T. For *RVH*: right ÂQRS deviation, high R in proportion to S on Leads V_1-V_2, with persistent S on Leads V_5-V_6. Secondarily considered were: QRS > 0.12 sec., intrinsicoid deflection > 0.035 sec. on Leads V_1-V_2, secondary changes of ST-T.

in Group I who showed this alteration was a 68-year-old man with severe scleroderma of the skin, of rapid evolution (7 months). This patient was not hypertensive.

Finally, a *notching of the P wave on standard leads*, mainly on Lead D_2, was frequently observed. The notch was either on the ascendant branch or at the top of P, resembling the "mitral" P wave, but without the increase in length beyond 0.11 second. The interval between peaks never exceeded 0.04 second (Figs. 5 and 6). According to Thomas and Dejong,[16] this type of notched P could still be normal; however, they found it exclusively in chest leads, especially the so-called "second peak type" where the second peak is higher. In Group I, 45.2 per cent and in Group II, 60.8 per cent, including all the autopsy cases who had had normal sinus rhythm (6 of the 7), presented this alteration. In such instances, postmortem examination always showed some pathology involving the auricular myocardium, namely, interstitial fibrosis, endocardial thickening, accumulation of collagenous tissue, dilation of the fibers, or calcification.

Obviously, any of these alterations represents an obstacle to the spread of the normal electrical stimulus, and notching of the P wave may appear. Although this finding does not indicate a specific type of injury, its high incidence in this series could lead to the suspicion of myocardial involvement by the disease.

2. *Pulmonary Pathologic Changes.*—When scleroderma has involved the lungs, alterations in structure and function, such as increase of the collagen connective tissue with alveolar thickening, compensatory emphysema, and, in some cases, rupture of the interalveolar septa with cyst formation, may result.[1,3,8,11,12,14,17] If these disturbances are extensive enough, physiopathologic changes take place, e.g., alveolar-capillary block, respiratory and ventilatory failure, anoxia, pulmonary arterial hypertension, and, finally, chronic cor pulmonale. This latter entity has been identified by the electrocardiogram in some patients with scleroderma lung disease, by tall peaked P waves on Leads D_2 and D_3, negative P wave on Lead V_L, and by a shift of $\hat{A}P$[2,4] and $\hat{A}QRS$[2,3,5,8] to the right in direct relationship with the degree of pulmonary hypertension and right ventricular overloading developed.

However, in the present series, only one patient, who had extensive scleroderma of the lungs corroborated at autopsy, showed an important shift of $\hat{A}P$ and $\hat{A}QRS$ to the right ($\hat{A}P$ from 0° to +90°, and $\hat{A}QRS$ from +70° to +90°) in 3 years of evolution. It is possible that in several patients with pulmonary involvement, but also with myocardial fibrosis, opposite forces are acting on both ventricles, preventing any shift of the electrical axis (Fig. 2).

We found two clinical instances of marked pulmonary fibrosis and chronic cor pulmonale among the patients in Group II (6.9 per cent); in both, the ECG showed evidence of right ventricular hypertrophy, and one of them also had the typical Q wave on Lead V_1, described by Sodi-Pallares and associates[18] in cases of right atrial dilatation. The autopsy findings in this particular case confirmed the electrocardiographic diagnosis.

One patient in Group I also presented electrocardiographic changes suggestive of right ventricular hypertrophy. This 37-year-old woman showed this

finding as well as low voltage after 1½ years of evolution of the scleroderma. She died at home 1 month later.

3. *Disturbances of the Conducting Medium.*—Skin thickening of the thoracic cage, pleural or pericardial fibrosis, and, especially, the presence of pericardial or pleural effusion, may produce a short-circuiting action, and a *low voltage of the tracing.* Nevertheless, in most of the cases reported,[2-6] as well as in our own experience, the principal cause of low voltage was merely myocardial fibrosis, as mentioned above. Pericardial effusion has been found in some instances.[1,13] Among our 12 cases with low voltage, only one patient had a significant amount of fluid in the pericardial sac. Another had bilateral pleural effusion. One patient with fibrinous pericarditis did not show a decrease in the voltage of the ECG. It is important to recognize the electrical position of the heart "S_1-S_2-S_3,"[19] because it may be the cause of the low voltage in some normal cases.

4. *Renal Involvement by the Disease.*—Renal involvement by the disease is not a rare complication. Piper and associates[14] found it in 74 per cent of their series of 31 cases with autopsy. Specific renal lesions have been described[20]: dilatation and mucoid intimal thickening of the larger intralobular arteries, with subsequent development of fibrinoid necrosis in the smaller arteries; often the affected arteries contain thrombi. There also may be found necrosis of the parenchyma, infarcts in the renal cortex, and wire-loop changes in the glomeruli.

When impairment of the kidney is great enough, hypertension or renal failure with metabolic disturbances can develop. The effect of these conditions on the heart may be reflected by the ECG showing left ventricular hypertrophy with or without evidence of systolic overloading,[21,22] or changes in Q-T or T due mainly to hypocalcemia or hyperkalemia.

However, hypertension and renal failure usually appear terminally in scleroderma, and there is often insufficient time for the development of secondary changes.

In 8 of our patients in Group II (27.6 per cent) the possibility of renal involvement was suspected. In 4 of these, such diagnosis was confirmed by autopsy. The remaining 4 had hypertension, and one of these also had uremia. Nevertheless, we could not rule out the association of essential hypertension with scleroderma. In 4 of the 8 cases there was electrocardiographic evidence of left ventricular hypertrophy. None presented metabolic changes.

SUMMARY AND CONCLUSIONS

The electrocardiograms of 60 patients with scleroderma were studied. The patients were divided into two groups: those *with* and those *without* apparent visceral involvement with the disease. Seven of the latter group died and autopsy was performed.

In Group I (*without* apparent visceral involvement) the ECG was normal in almost 75 per cent of the cases. However, 25 per cent showed definite pathologic alterations, bespeaking myocardial damage, despite the absence of clinical evidence. The evolution time of the disease in these cases varied between 7 months and 15 years.

In Group II (*with* visceral localization of the disease) the ECG was fairly abnormal in slightly more than 75 per cent of cases, including 2 cases without clinical diagnosis of heart disease. Of the remaining 25 per cent, only one case (3.4 per cent) with a clinical and radiologic diagnosis of cardiopathy presented a normal ECG.

The most frequent alteration in all cases was notching of the P wave on standard leads. Because of its high incidence among all patients, and the presence of auricular pathology in the autopsy cases, the authors consider that this finding creates the suspicion of myocardial damage by scleroderma.

Besides this, the following electrocardiographic findings had the highest incidence, all of them among the patients in Group II: left ventricular hypertrophy (34.5 per cent), low voltage (27.6 per cent), incomplete right bundle branch block (20.7 per cent), subepicardial ischemia (17.2 per cent). Right ventricular hypertrophy, incomplete left bundle branch block, complete A-V block, right or left auricular enlargement, prolonged Q-T, subendocardial lesions, focal peripheral block, and extrasystoles were also found occasionally, but with low incidence.

This analysis suggests that of all mechanisms which may act on the ECG in generalized scleroderma, myocardial fibrosis is the most important.

A review of the literature as well as an anatomic, physiopathologic, and clinical correlation have been presented.

The authors wish to thank Dr. Irving S. Wright for his kind review of and suggestions for this report.

REFERENCES

1. Weiss, S., Stead, E. A., Jr., Warren, J. V., and Bailey, O. T.: A.M.A. Arch. Int. Med. **71**:748, 1943.
2. Goetz, R. H.: Angiology **2**:555, 1951.
3. Goldman, I. R., Young, J. M., and Knox, F. H.: Dis. Chest. **25**:94, 1954.
4. Hurly, J., Coe, J., and Weber, L.: Am. Heart J. **42**:758, 1951.
5. Mustakallio, K. K., and Sarajas, H. S. S.: Am. Heart J. **47**:437, 1954.
6. Weinberg, S. L., Reynolds, R. W., Rosenman, R. H., and Katz, L. N.: Am. Heart J. **40**:745, 1950.
7. Barritt, D. W., and O'Brien, W.: Brit. Heart J. **14**:421, 1952.
8. Spain, D. M., and Thomas, A. G.: Ann. Int. Med. **32**:152, 1950.
9. Zuckerman, R., Medrano, G., Bisteni, A., and Ortiz, J. A.: Arch. Inst. cardiol. México **21**:30, 1951.
10. East, T., and Oram, S.: Brit. Heart J. **9**:167, 1947.
11. Leinwand, I., Duryee, A. W., and Richter, M. N.: Ann. Int. Med. **41**:1003, 1954.
12. Beerman, H.: Am. J. Med. Sc. **216**:458, 1948.
13. Mathisen, A. K., and Palmer, J. D.: Am. Heart J. **33**:366, 1947.
14. Piper, W. N., and Helwig, E. B.: A.M.A. Arch. Dermat. **72**:535, 1955.
15. Robles Gil, J.: Ann. Int. Med. **34**:862, 1951.
16. Thomas, P., and Dejong, D.: Brit. Heart J. **16**:241, 1954.
17. Wigley, J. E. M., Edmunds, V., and Bradley, R.: Brit. J. Dermat. **61**:324, 1949.
18. Sodi-Pallares, D., Bisteni, A., and Herrmann, G. R.: Am. Heart J. **43**:716, 1952.
19. Vizcaíno, M., Sodi-Pallares, D., and Cabrera, E.: Arch. Inst. cardiol. México **14**:261, 1944-1945.
20. Moore, H. C., and Sheehan, H. L.: Lancet **1**:68, 1952.
21. Cabrera, E., and Monroy, J. R.: Am. Heart J. **43**:661, 1952.
22. Cabrera, E., and Monroy, J. R.: Am. Heart J. **43**:669, 1952.
23. Windesheim, J. H., and Parkin, T. W.: Circulation **17**:874, 1958.

Combined Auricular and Ventricular Septal Defects: A Study of Five Cases, With Postmortem Confirmation in Three

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Auricular septal defect (ASD) is the second most common congenital cardiac malformation in our experience.[1,2] The association of ASD with other congenital or acquired malformations, namely, with anomalous venous return[3] and rheumatic mitral disease,[4] is not uncommon. In these cases, ASD is often the principal malformation. When it is associated with other, more complex congenital anomalies, ASD constitutes a lesser anatomic feature within the complex physiopathologic picture of the disease, such as in pentalogy of Fallot.

Ventricular septal defect (VSD) is the third most common congenital cardiac malformation in our experience (about half as frequent as ASD). The association of this malformation with other anomalies is perhaps less common. However, just as in the case of ASD, VSD may be one of multiple malformations wherein its physiopathologic expression is a more or less important feature of the anatomic and clinical picture.

In our experience the association of these two defects is unusual. It is not easy to determine which of the two defects is the more important in the clinical picture which they originate when associated. It seems to be a combination of physiopathologic features in which each defect contributes in approximately equal proportions. The identification of both defects is difficult, so that a specialized method may be the only means of solving the problem.

We have been unable to find much literature on the subject. Abbott,[5] for example, does not mention ASD associated with VSD except under the heading "fetal passages," thus rendering it difficult to ascertain the nature of the ASD, which might very well be a patent foramen ovale. Gasul and associates,[6] in 1953, reported 4 cases with this association, but only 2 of these had large ASD, while 2 others had a probe-patent foramen ovale.

The purpose of this paper is to report 5 cases of this unusual association, 3 of which have autopsy reports. An attempt is made to evaluate the importance of clinical, radiologic, and electrocardiographic findings prior to the use of specialized studies and to surgical correction of the defects.

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TABLE I. CLINICAL DATA

CASE, AGE, SEX	HISTORY OF RESPIRATORY INFECTIONS OR BRONCHO-PNEUMONIA	HEART FAILURE	DYSPNEA ON EFFORT	HEMOPTY-SIS	CYANOSIS	ACCENTU-ATED P_2	SYSTOLIC MURMUR	MID-PRECORDIAL SYSTOLIC THRILL	LOCATION OF APEX	OBSERVATIONS
1. O.M. 10 yr. F	yes	yes	yes	yes	no?	+++	2, 3, 4, 5 LIS	3, 4, 5 LIS	6 LIS	Died postoperatively in heart failure
2. H.G. 18 yr. M	no	no	yes	yes	no	++	3, 4 LIS	3, 4 LIS	5 LIS	Died with subacute bacterial endocarditis
3. V.C. 6 yr. M	no	no	no	no	transient in infancy	++	4 LIS	no	4 LIS	Living and well
4. L.H. 5 yr. M	yes	no	no	no	no	+	3, 4 LIS	no	4 LIS	Living and well
5. H.I. 1 mo. F	terminal broncho-pneumonia	yes	yes	no	yes	++	3, 4 LIS	no	?	Mongoloid. Died in heart failure and with bronchopneu-monia

LIS = left intercostal space.

MATERIAL AND METHODS

Our 5 patients ranged in age between 1 month and 18 years. There were 2 females and 3 males. Three of the patients died and were autopsied. Three were catheterized and one of these had an angiocardiogram. One patient was operated upon unsuccessfully. All had clinical, radiologic, and electrocardiographic studies. The clinical data are plotted in Table I.

DISCUSSION

Embryology and Anatomy.—The three autopsy specimens belong to the subjects who were aged 1 month, 10 years, and 18 years. ASD in the three cases were widely patent foramina ovalii. These seem to have been the result of excessive resorption of the septum primum and faulty development of the septum secundum[7] (Figs. 1 and 2). Measurements in the smallest heart were not accurate, but the defect appeared as a wide one and not as a probe-patent foramen ovale. The defects were always highly placed, in respect to the mitral and tricuspid valves. In the two living cases the ASD was proved by catheterization, and on purely statistical grounds we assume that the defects belong to the same embryologic type as that in the autopsied cases, since it is the most common type found in autopsy specimens and at operation.[2]

De la Cruz and associates[8] have recently classified VSD into two main types: basal and medial. The former originate through lack of development of the

Fig. 1.—The ventricular septal defect in Case 1, as seen from the right side, and the auricular septal defect. The latter is shown above with a probe. Note the proximity of the ventricular septal defect to the septal leaflet of the tricuspid valve.

pars membranacea, and they are adequately subdivided into basal anterior (Type 1), basal medial (Type 2), and basal posterior (Type 3). Type 1 is located in front of the crista supraventricularis and Type 2 behind this structure, immediately under the aortic semilunar valve cusps. Two of our cases (Cases 1 and 2) belonged to Type 2 of this classification, while Case 5 belonged to Type 1. In no case did the aorta override the interventricular septum. The size of the largest defect (Case 2) measured 6 mm. in diameter, and the edge of the defect showed vegetations of bacterial endocarditis.

Although a correct anatomic classification of the VSD in the two clinical cases is not possible, there is reason to believe they are due to absence of the pars membranacea. Clinical and hemodynamic behavior seem to substantiate this assumption.

The histories of the patients point out the presence of pulmonary congestion of varying degrees: severe in Cases 1, 2, and 5 (the autopsied cases) and mild to moderate in the other two. This was the basis of severe lower respiratory infections leading to transient bouts of right ventricular failure in Case 1; marked accentuation of the second pulmonic sound in Case 2; bronchopneumonia in Case 4; and terminal bronchopneumonia in Case 5. Pulmonary congestion was apparently due to predominant, or perhaps exclusive, arteriovenous shunts. One might reason that the pressure of the right ventricle was, at some stage, considerably elevated in the three patients who showed cyanosis with effort (Cases 2, 3, and 5), that is, a transient inversion of the shunt took place through one of the spetal defects, probably the VSD.

The site of the cardiac murmur in these patients was consistent with the diagnosis of VSD. It was heard in every case at the fourth left intercostal space. The intensity and harshness of the murmur were other features compatible with this diagnosis. Yet, a palpable thrill was only noted in two cases.

Fig. 2.—Case 2 from the right cavities. The ventricular septal defect is shown by the arrow. Vegetations of bacterial endocarditis were present.

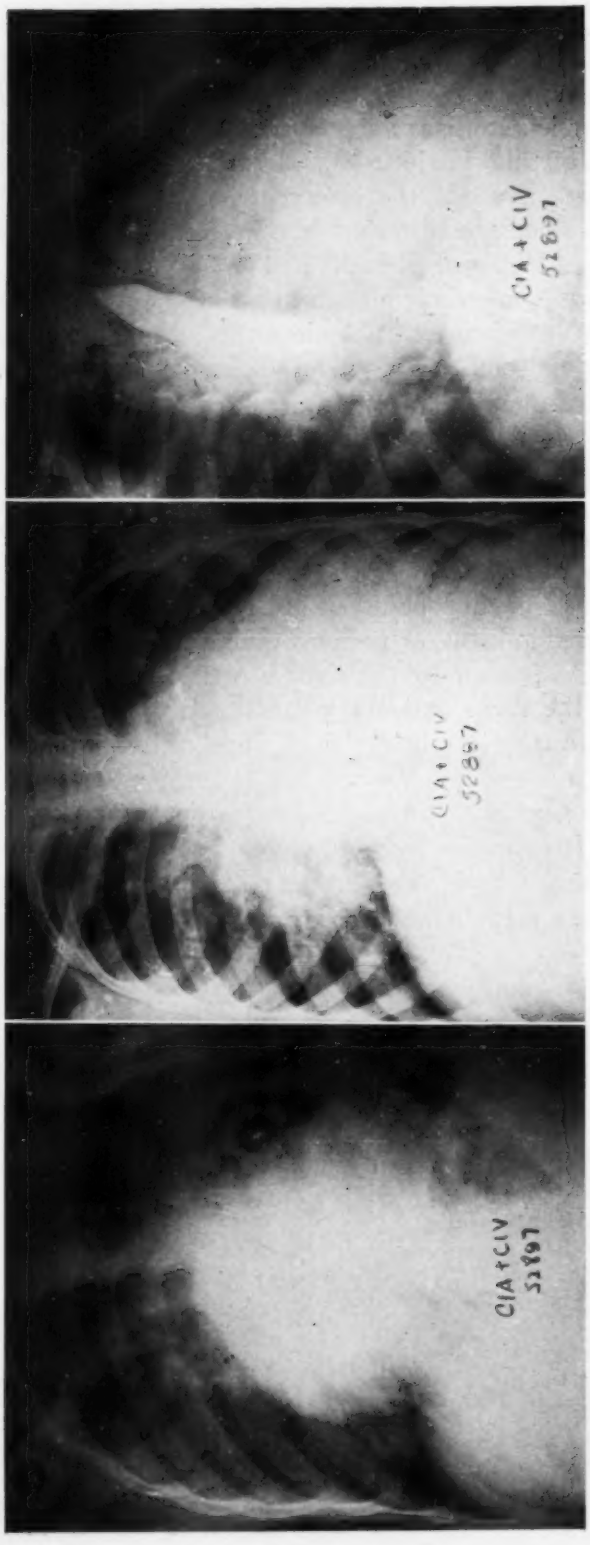

Fig. 3.—Frontal and oblique views of Case 1. Note the large pulmonary artery in the frontal view, as well as the profuse pulmonary circulation. The right oblique view shows slight left auricular enlargement. The left oblique view shows left ventricular enlargement. Cardiomegaly is readily apparent.

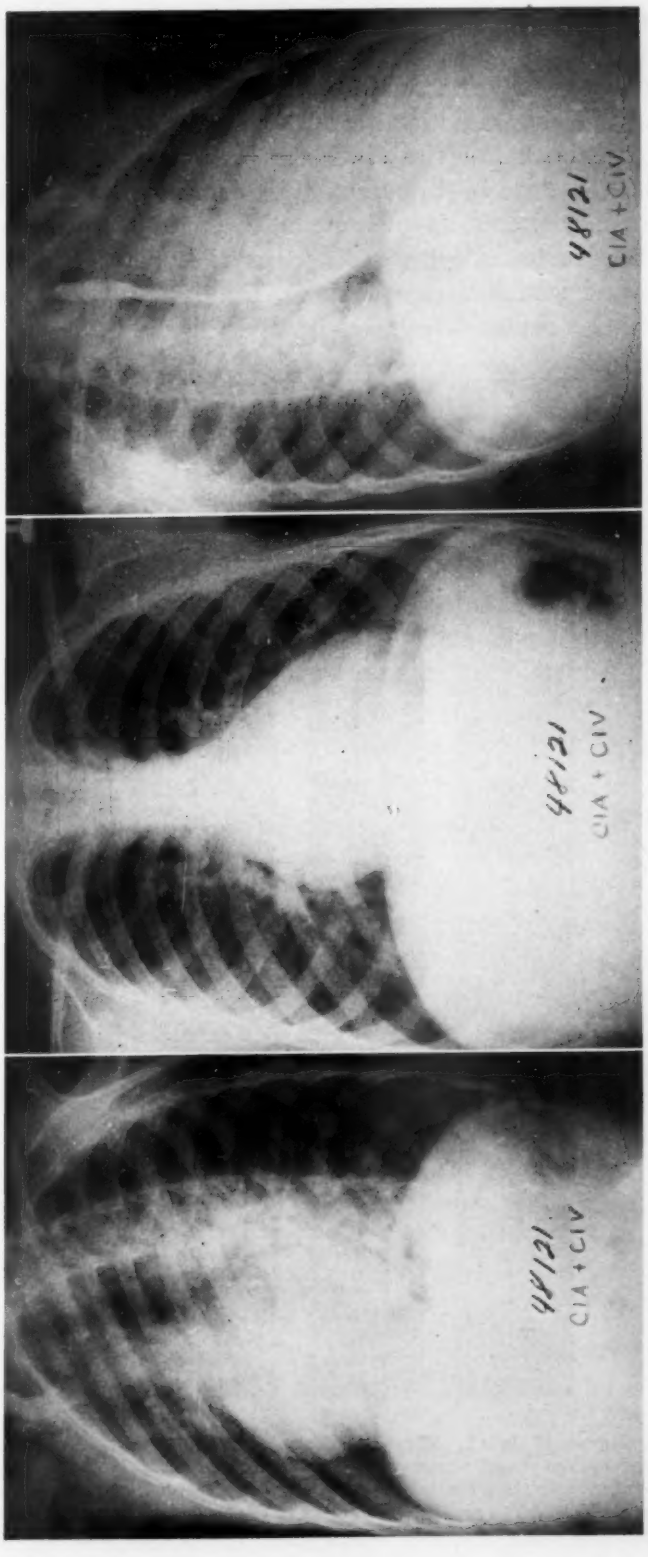

Fig. 4.—X-rays of Case 3. Notice the nearly normal size of the heart. The pulmonary artery is normal. Lung vascularity is not increased, and in the left oblique view there is suggestion of right ventricular enlargement.

Clinically, the diagnosis of VSD was correct in one of the autopsy cases (Case 2), and the diagnosis of ASD was correct in two of the living cases. Yet, this defect was thought to have unusual features in Case 1, such as the harshness of the murmur and its wide radiation from the second to the fourth left intercostal spaces. For this reason the diagnosis of atrioventricularis communis (AVC) was postulated. Also in support of this view was the important hypertension of the pulmonary circuit, an uncommon feature in isolated ASD. Hemodynamic data forced us to accept the diagnosis of hypertensive ASD in this case. But ASD alone was not responsible for the hypertension; it was due to the presence of the other septal defect. Hemodynamic data in Case 3 led to the

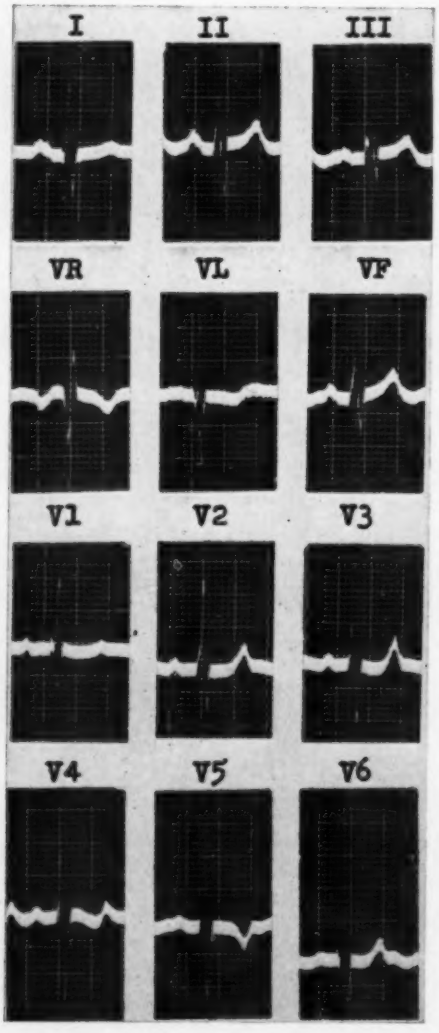

Fig. 5.—Electrocardiogram of Case 1. There is a left axis deviation. Left auricular enlargement is evident because of slurred and notched P waves in Lead I. Its duration is 0.12 second. The rsR complex in Lead V_1 is suggestive of incomplete RBBB. Biventricular hypertrophy is present. The rsR complex in Lead V_1 and RS in Leads V_2 and V_3 (with initial slurring of the ascending branch of R) are due to right ventricular enlargement. The type of complexes seen in Leads V_5 and V_6 portray left ventricular hypertrophy.

suspicion of a defect of the ostium primum type or an AVC. Underdevelopment, feeding problems in infancy, frequent respiratory infections, and cardiac failure are not uncommon complications in AVC.[13,14] Therefore, the diagnosis of this malformation made in two of our cases had reasonable clinical basis. This means that combined VSD and ASD are capable of producing the picture often seen in AVC. Yet, on clinical grounds it would be difficult to suspect both defects.

It was not difficult to diagnose the VSD in Case 2 on the basis of the clinical findings (this patient was not catheterized). Bacterial endocarditis gave strong support to the diagnosis. Furthermore, this complication would have ruled out the diagnosis of ASD had it been suspected, because of its great rarity in such cases.

The cases reported by Gasul and associates,[6] in which the premortem diagnosis was not stated, often had the same clinical features: signs of pulmonary congestion, cardiomegaly, harsh systolic cardiac murmurs, and accentuation of the second pulmonary sound. These workers believe that the association of defects produced a distinct clinical syndrome which was severe enough in their patients so that none reached 6 months of age. While we agree that the presence of two shunts places a great load on the heart, our cases (with one exception) tolerated their malformation for several years.

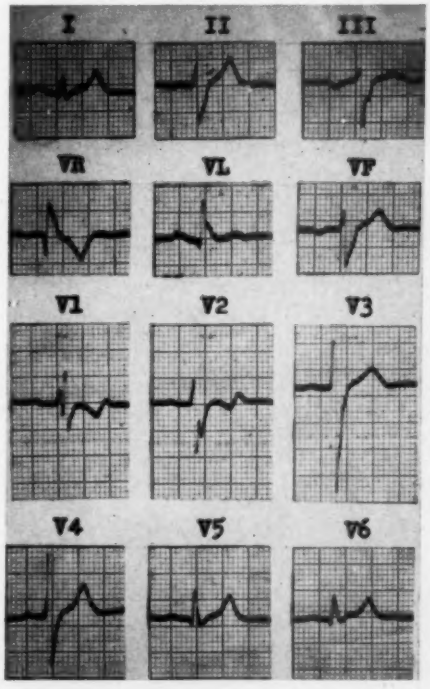

Fig. 6.—Electrocardiogram of Case 2. There is left axis deviation at −50°. First degree A-V block is present since the P-R interval measures 0.20 second. Biventricular hypertrophy is evident together with RBBB. The rsRs complex portrays activation of the trabecular zone of the right ventricle. RS complexes with slurred S waves in Leads V_2, V_3, and V_4 correspond to the activation of the apex of the left ventricle. The qRs complexes with slurred S wave in Lead V_5 and V_6 represent the activation of the free wall of the left ventricle.

Radiologically, we observed varying degrees of cardiomegaly (Figs. 3 and 4) due to hypertrophy and dilatation of the right cardiac chambers and, to a certain extent, of the left ventricle. This picture was compatible with the clinical diagnosis of VSD. Indeed, the left cardiac chambers are not usually enlarged in isolated ASD, while this finding is a usual feature in VSD or in AVC. Because of this, Case 1 was thought to have an ostium primum defect or, perhaps, an AVC.

In every case the pulmonary artery and the hilar shadows were markedly enlarged and pulsating. This behavior was the expression of an important left-to-right shunt, possibly at both auricular and ventricular levels. This view was substantiated by hemodynamic findings. The cardiomegaly was estimated in 4 patients at between 45 and 58 per cent. Therefore, the malformations were not placing a tremendous load on the heart as in Gasul and associates' patients, where a cardio-thoracic ratio of 70 per cent was obtained in one instance.

Angiocardiography was a useful diagnostic method. It was performed in Case 3, and it demonstrated both defects. The heart in this case was almost normal in size.

Electrocardiographically, four patients showed the following salient features: (1) left axis deviation; (2) right bundle branch block (RBBB), i.e., rsR, rsRS, and RS (with slurring of the ascending branch of R) type complexes in the right precordial leads, and RS (with slurring of the S wave) and qRs (with slurring of the S wave) complexes in the left precordial leads; (3) biventricular hypertrophy with systolic overloading of the right ventricle and diastolic overloading of the left ventricle.[9,12] The 1-month-old patient had only right ventricular enlargement with systolic overloading (Figs. 5 and 6).

The electrocardiographic pattern of ASD has become well known since being pointed out by Routier and Brumlik.[10] Later, Vizcaino and associates[11] insisted on the high incidence of RBBB in ASD. Other usual features are right axis deviation, conduction disturbances expressed as first degree A-V block, and suggestive evidence of right ventricular hypertrophy.

In VSD the more constant electrocardiographic features are those which portray biventricular hypertrophy and RBBB, the latter, however, less often than in ASD. Ample deflections in precordial leads are frequent.

Therefore, in spite of the presence of common electrocardiographic features, there are differences which one is able to recognize for each individual defect. This is why the tracings are bizarre and suggest a combination of electrocardiographic disturbances seen in AVC. This is so because, anatomically, AVC is a combination of ASD plus VSD. There seems to be only a difference of degree, hemodynamically speaking, between AVC and our cases of ASD plus VSD. Thus, the electrocardiographic pattern is reminiscent of that seen in AVC, either complete or partial.[14] In any case, the tracings are not suggestive of pure ASD, although these features could occasionally be seen in some cases of VSD. Toscano-Barbosa and associates[15] have recently stated that the electrocardiographic pattern of AVC is quite characteristic, the principal features being: (1) P-R prolongation time, (2) left axis deviation, and (3) biventricular hypertrophy. These authors very aptly conclude, however, that these patterns cannot be considered pathognomonic. Our cases afford confirmatory proof of this statement.

Catheterization.—Catheterization data are presented in Table II. The ASD was entered with the catheter only in Case 1. The VSD was not catheterized in any case.

Gas analysis in the three catheterized cases shows a step-up of two volumes of oxygen at the level of the right auricle. A new step-up of nearly two volumes of oxygen was found at the ventricular level in Cases 3 and 4, and of only one volume in Case 1. In the latter case, temporary occlusion of the ASD by means of a Dotter-Lucas catheter still permitted increase in oxygen saturation at the ventricular level. These findings in the first two cases are suggestive of the double defect, and could be compatible with AVC. In Case 1 the slight step-up after occlusion of the ASD was erroneously thought to be due to the presence of a pulmonary vein with anomalous connection to the right auricle.

TABLE II. CATHETERIZATION DATA

CASE, AGE	GAS ANALYSIS						PRESSURES (MM. Hg)			
	VOLUMES OF OXYGEN (%)									
	SVC	RA	RV	PA	LA	PA#	RV	PA	PA#	PULMONARY FLOW (L./MIN.)
1. O.M. 10 years	8.55	11.25	12.30	11.90	13.90	13.50 86.3%	89 — 4.2	90 — 49	101 — 67	11.88
3. V.C. 6 years	11.75	14.05	15.96	15.50	—	18.7 98.4%	31 — 1	29 — 9	—	3.60
4. L.H. 5 years	7.99	9.96	11.95	11.95	—	12.36 97.2%	35 — 2.4	28 — 7.1	61 — 39	5.41

SVC = Superior vena cava. RA = Right auricle. RV = Right ventricle. PA = Pulmonary artery. PA# = Peripheral artery.

The highest ventricular pressure was seen in Case 1 (90 mm. Hg systolic). Cases 3 and 4 had slight increase of right ventricular pressure (31 and 35 mm. Hg systolic). Correlation of these data with pulmonary flow determinations seems to indicate that great pulmonary flow was the cause of pressure elevation in the pulmonary circuit of Case 1 (see Table II). Conversely, small pulmonary flow as in Cases 3 and 4 hardly had any effect on pulmonary pressure. A great pulmonary flow in Case 1 could have been anticipated in view of the cardiomegaly (Fig. 3). The enlargement of the heart was mainly at the expense of the right cardiac chambers, that is, the portion of the heart receiving the volume of blood shunted through the septal defects. The left ventricle was also enlarged because of the loss of blood in each contraction, and because all the shunted blood returned eventually to the left cardiac chambers.

Arterial blood saturation was in the lower limits of normal (for Mexico City) in Case 1; it could perhaps be considered abnormal despite absence of visible cyanosis. The presence of a mixed shunt should be considered in this case.

In summary, from the hemodynamic standpoint our cases mimic AVC inasmuch as there were two oxygen step-ups: one at the auricular level and one at the ventricular level, which are salient diagnostic points in the diagnosis of AVC in the experience of some workers.[16]

Surgical Comment.—Case 1 was unsuccessfully operated upon, with the diagnosis of ASD, probably of the AVC type. The basis for this diagnosis has been outlined. The operation seemed justified in view of cardiomegaly, pulmonary hypertension, and the fact that the shunt was mainly left-to-right. The closure of the ASD alone might have afforded benefit to the patient. Severe rhythm disorders rendered the operation impracticable, and the patient made a poor recovery after thoracotomy, dying a few weeks later in heart failure. Fibrinous pericarditis was a major contributory cause of death.

The living patients are quite young, and for this reason as well as for lack of cardiac enlargement or pulmonary hypertension, the smallness of the shunts, and the patients' excellent tolerance of the malformations, these cases do not seem to justify operation.

SUMMARY

The authors studied five cases of the unusual association of auricular septal defect combined with ventricular septal defect. In three cases autopsy studies, were made and in one of these and in two others catheterization studies were performed. Still one more had an angiocardiogram. The authors discuss the subject from the embryologic, clinical, radiologic, electrocardiographic, and hemodynamic standpoints. They emphasize the difficulties of differential diagnosis with cases of persistent atrioventricular canal.

REFERENCES

1. Espino-Vela, J.: Unpublished observations.
2. Méndez-Aponte, J.: Estudio de 110 Casos Confirmados de Comunicación Interauricular. Tesis Recepcional, México, 1958, Instituto Nacional de Cardiología.
3. Canale, M., Espino-Vela, J., and Rubio, V.: La Desembocadura Anómala de Venas Pulmonares. (To be published.)
4. Espino-Vela, J., Mata, L. A., and Torpey, A.: Arch. Inst. cardiol. México **27**:411, 1957.
5. Abbott, M.: Atlas of Congenital Cardiac Disease, New York, 1936, American Heart Assn.
6. Gasul, B. M., Weiss, H., Fell, E. H., Dillon, R. F., Fisher, D. L., and Marienfeld, C. J.: A.M.A. Am. J. Dis. Child. **85**:404, 1953.
7. De la Cruz, M. V.: Personal communication.
8. De la Cruz, M. V., Christie, F., and Pérez-Olea, J.: Arch. Inst. cardiol. México **28**:358, 1958.
9. Sodi-Pallares, D., and Marsico, F.: AM. HEART J. **49**:202, 1955.
10. Routier, D., Brumlik, J., and Malinsky, A.: Arch. mal. coeur **33**:40, 1940.
11. Vizcaino, M., Vaquero, M., and Pellón, R.: Comunicación Interauricular. Estudio de 20 Casos, Chicago, 1948, III Congreso Interamericano de Cardiología.
12. Cabrera, E., and Monroy, J.: AM. HEART J. **43**:669, 1952.
13. Blount, S. G., Balchum, O. J., and Gensini, G.: Circulation **13**:499, 1956.
14. Brandenburg, R. O. and Dushane, J. W.: Proc. Staff Meet. Mayo Clin. **31**:509, 1956.
15. Toscano-Barbosa, E., Brandenburg, R. O., and Burchell, H. B.: Staff Meet. Mayo Clin. **31**:513, 1956.
16. Wakai, C. S., Swan, H. J. C., and Wood, E. H.: Staff Meet. Mayo Clin. **31**:500, 1956.

Pneumococcal Endocarditis

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Pneumococcal endocarditis is a septic complication of acute pneumococcal infections, most commonly pneumococcal pneumonia. Although the pathologic entity was first described more than one hundred years ago,[1] very little clinical recognition, or even suspicion, was accorded to this complication of pneumococcal infections until relatively recent times, when the biology of the pneumococcus was more fully understood. Even during the era of specific serum therapy of the pneumonias, endocarditis was most frequently recognized at necropsy and reported as a reason for failure of serotherapy. The introduction of antimicrobial agents of both synthetic and natural origin during the past 20 years has been responsible for a very dramatic reduction in mortality from the pneumococcal pneumonias; also, these agents have reduced the incidence of purulent complications of these pneumonias and, in many instances, have been responsible for the cure of complications which at one time were considered almost universally fatal. In view of the fact that agents are available for the treatment of such complications, a review of the literature on pneumococcal endocarditis was made in the hope that a better appreciation of the clinical features of the disease entity might be made available, thereby permitting therapy to be instituted earlier.

A search of the published literature disclosed reports of almost 600 cases of endocarditis caused by the pneumococcus. Cases were excluded when the organism was identified only by its morphologic and tinctorial characteristics. In this connection, it must be deplored that hospitals and laboratories have permitted the use of pneumococcus typing sera to become obsolescent, if not obsolete. By means of these sera the pneumococcus can be identified rapidly and classified as to type without resort to painstaking laboratory methods; moreover, the use of such sera constitutes an ideal ecologic tool by virtue of the "self-tagging" of the capsular carbohydrate of the pneumococcus.

It has not been possible to ascertain the relative importance of the pneumococcus as the causative agent in acute endocarditis. Whenever relative figures were reported, it appeared that the pneumococcus and *Staphylococcus aureus* were about equally responsible for cases of acute endocarditis. During the period 1936-1941, the pneumococcus caused many more cases of acute endocarditis among adults in the wards of the Cincinnati General Hospital than did the staphylococcus.

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Of the reported cases, the distribution by types may be seen in Table I. While Type I predominates among the typed cases, several other types deserve consideration because of the relatively frequent incidence in being associated with endocardial lesions. Moreover, by all odds, Type I was the most frequent causative agent of pneumococcal pneumonia, and it is, therefore, not surprising to note the high incidence of endocarditis, as well as of other complications, due to this type. In view of the great incidence of, and mortality among, cases of pneumonia caused by Type-III pneumococcus, especially during the presulfonamide period, it is strange that only 16 cases of Type-III endocarditis have been reported. It is possible that bacteremic infections due to this organism pursued such a rapidly fatal course that the development of endocardial lesions was thereby precluded. If the production of antibodies is a factor in the pathogenesis of endocarditis,[2] this factor may be pertinent, for the Type-III pneumococcus was considered a relatively poor antigen. The reasons for the invasion of the blood stream by the pneumococcus are not known, but great variations in the incidence of the bacteremia in pneumonia have been recorded by Bullowa and Wilcox,[3] as well as others. Such factors may probably eventually explain many unanswered questions regarding the biology of the pneumococcus. Attention should be called to the relatively great incidence of endocarditis caused by Types II, V, VII, and XII. The incidence of Types II and V in endocarditis was not unexpected, for these organisms showed a great tendency to be associated with bacteremia when causing pneumonia. On the other hand, Type VII had a relatively low incidence in bacteremic pneumonia but ranked third among the types in the incidence of endocarditis. Still more unexpected was the number of cases caused by Type XII. This organism causes pneumonia relatively infrequently, but 15 cases of endocarditis have been reported and almost half of these were observed at the Cincinnati General Hospital within a period of 5 years.

Pneumococcal endocarditis has been reported among all age groups. While there have been several case reports of patients in their first as well as ninth decades, the median age incidence lies in the fifth decade. An inspection of

TABLE I. DISTRIBUTION OF PNEUMOCOCCUS TYPES

TYPE	NUMBER OF CASES	TYPE	NUMBER OF CASES	TYPE	NUMBER OF CASES
I	73	XII	15	XXIII	4
II	42	XIII	3	XXIV	1
III	16	XIV	9	XXV	5
IV	12	XV	2	XXVII	2
V	17	XVI	1	XXVIII	1
VI	9	XVII	—	XXIX	3
VII	20	XVIII	11	XXXI	—
VIII	12	XIX	3	XXXII	1
IX	2	XX	5	> XXXII	2
X	3	XXI	—	Gr.IV	33
XI	3	XXII	3	Untyped	280

Total Number of Cases: 593

Table II will quickly disclose that the age pattern is dissimilar from that seen in subacute bacterial endocarditis, which is usually observed in the younger age groups.

Neither sex nor race seems to have a predisposing influence on the incidence of pneumococcal endocarditis. The complication was noted much oftener in males than in females, but likewise the primary disease, pneumococcal pneumonia, is seen much more frequently in males. Similarly, pneumonia is seen in large hospitals of the north temperate zone more often in Negroes, although the incidence of endocarditis is no greater among Negroes than among white pneumonia patients.

While pneumococcal endocarditis may follow any primary pneumococcal infection, the overwhelming majority of the reported cases followed pneumococcal pneumonia, usually of the classical lobar type. Less frequently, the pneumonia was of the lobular type or may have been diagnosed only at necropsy. In the rare instance, the portal of entry was difficult to ascertain; endocarditis due to a pneumococcus has been reported to follow meningitis, mastoiditis, tooth extraction, septic abortion, urethral dilatation, and surgical intervention for various conditions.

It is doubtful if antecedent disease of the valvular endocardium predisposes to attack by the pneumococcus. In this series of cases collected from the literature a history of rheumatic heart disease or physical signs of valvular damage were noted in less than 10 per cent of the cases. On the other hand, considerably more cases were shown at necropsy to have histological stigmata of rheumatic fever. It may be safely concluded that there does not appear to be nearly so great a predisposition of antecedent valvular damage to attack by the pneumococcus as has been shown to be true in the case of *Streptococcus viridans* and related groups of streptococci. While an occasional case of pneumococcal endocarditis has been reported as being engrafted on a valve damaged by syphilis, this complication happens only very rarely.

Although acute endocarditis has been produced in experimental animals, the pathologic picture analogous to that seen at necropsy cannot be duplicated with regularity; consequently, the pathogenesis of the human disease remains

TABLE II. AGE DISTRIBUTION

DECADE	NUMBER OF CASES
1–10	17
11–20	19
21–30	53
31–40	82
41–50	92
51–60	75
61–70	35
71–80	16
81–90	2
Total:	391

conjectural. Wadsworth[4] remarked on the close similarity of the endocardial lesions of horses which had been immunized against the pneumococcus to those of human beings with pneumococcal endocarditis; moreover, these lesions were much more frequent in animals which had a relatively high antibody content in their sera. Later, Keefer[2] drew attention to the similarity of the immunological status of human beings with pneumococcal endocarditis and Wadsworth's horses; in both species pneumococcemia and pneumococcal antibodies could be demonstrated simultaneously on many occasions. Keefer considered the antibody content significant, in that the clumping of bacteria thereby enhances their localization on the valve cusps. Such a thesis would tend to explain the relative paucity of endocardial lesions caused by Type III pneumococcus.

Other factors would have to be invoked to explain the localization of bacteria on one valve oftener than on another, or even on any physical obstruction to the flow of blood, such as a bifurcation. Table III summarizes the sites of localization of the cases detailed in the literature. Thus it can be seen that the valves of the left side of the heart were involved more than 5 times as frequently as those on the right; and in about 8 per cent of the cases both sides of the heart exhibited endocardial lesions. In endocarditis secondary to pneumonia it is not unreasonable to suspect that the bacterial content of the blood just returning from the lung may be greater than that returning to the right side of the heart, which could be a decisive factor in the tendency of pneumococcal endocarditis to preponderate on the aortic and mitral valves. Whether it is necessary to invoke the factors of impact, contact, and pressure as advocated by Allen[5] cannot be stated at this time. It seems certain, however, that vascular thrombosis is not a very important factor in the pathogenesis of this type of acute endocarditis.

The relative freedom of the tricuspid and pulmonary valves from endocardial lesions caused by the pneumococcus deserves comment. In this series of cases the aortic valve was involved 250 times and the mitral valve 237 times, whereas vegetations were observed on the tricuspid valve in 92 instances and on the pulmo-

TABLE III. SITE OF ENDOCARDIAL LESION

SITE	NUMBER OF CASES
Aortic Valve	169
Mitral Valve	156
Tricuspid Valve	59
Pulmonary Valve	13
Aortic and Mitral Valves	55
Aortic and Tricuspid Valves	11
Mitral and Tricuspid Valves	11
Aortic and Pulmonary Valves	3
Aortic, Mitral, and Tricuspid Valves	8
Mitral, Pulmonary, and Tricuspid Valves	1
Aortic, Mitral, Pulmonary, and Tricuspid Valves	2
Aortic, Mitral, and Pulmonary Valves	2
Ventricular Wall	7
Auricular Wall	1
Patent Ductus	1
Total	499

nary valve in only 21. On the other hand, Goldburgh, Baer and Lieber[6] reported that in their experience at the Philadelphia General Hospital the pneumococcus attacked the tricuspid valve alone relatively more often than did other organisms; yet, in the same series of 62 cases the pulmonic valve alone was not attacked in one case but was involved along with the mitral and tricuspid valves in another case. Such significant differences in the attack rates between the analogous valves and between the two sides of the heart lend support to Allen's thesis that impact, contact, and pressure are important factors in the pathogenesis of endocarditis of bacterial origin.[5]

In a single instance, endocardial lesions were noted only on the auricular wall, while in several cases such lesions were observed at necropsy to involve the ventricular wall, either alone or as an extension from valvular lesions. And in one case a patient with a patent ductus arteriosus is reported to have recovered after penicillin and ligation of the ductus.[7]

In view of the fact that more than 90 per cent of the cases of pneumococcal endocarditis represent complications of pneumococcal pneumonia, the clinical picture of the complication may be completely masked by the primary disease. While classical pneumococcal pneumonia may affect people of all ages, endocarditis is primarily a complication affecting patients of middle age and older. The complication is frequently ushered in by a sudden chill early in convalescence, at which time either relapse, recrudescence, or inadequate therapy may offer a plausible explanation to the physician for the chill and subsequent fever. At other times the complication apparently has its onset early in the febrile course of the patient and may thereby escape detection. In another group of patients the onset of the endocarditis comes late in the course of the disease or even after recovery from a presumably trivial respiratory infection; during the era of serum therapy the exacerbation of fever frequently required differentiation from serum sickness as an explanation therefor.

Although the patient may tolerate the chill and subsequent fever satisfactorily, there is usually an increase in the anxious appearance of the patient with an endocardial complication of pneumonia. Frequently, the evidence of increased toxemia is the principal sign to alert the physician to the diagnosis when no localizing signs are present.

Associated with pyrexia there is almost a tachycardia consistent with an infectious process of serious import. However, abnormal rhythm of the heart beat or pulse is unusual even late in the course of the disease. As in other forms of bacterial endocarditis, fibrillation is rare, although it may be observed as a sign of antecedent disease. Examination of the heart may disclose little deviation from the normal. Modest enlargement may be noted and is important when occurring under observation. Likewise, auscultation may disclose little of import. If the patient is still ill with pneumonia or meningitis, it may be impossible to perform a satisfactory auscultatory examination; however, if sounds are heard which indicate a change in the competence of any valve, the suspicion of endocarditis should be entertained seriously. In my experience, as well as in that of others, a diastolic murmur or thrill over the aortic area is confirmatory evidence of endocardial disease in a patient convalescing from pneumonia.

Of course, recordings of blood pressure consistent with aortic insufficiency may be noted in the patient with a well-advanced lesion of the aortic valve. Unfortunately, in more than half of the patients, auscultatory signs indicating endocardial mischief are absent. Petechiae and purpura have been reported in a relatively small per cent of the cases. Such findings were unexpected in view of the great incidence of these signs in subacute bacterial endocarditis. It is possible that lack of diligence in minute examination of a very ill patient may explain partially such an observation.

The gravity of the patient's condition may account for the infrequency with which a palpably enlarged spleen has been observed. At necropsy this organ is usually slightly enlarged, and its palpability during life has been remarked upon by a few clinicians.

On the other hand, meninigitis was noted in a majority of the reported patients either during life or at the necropsy. A relatively small per cent of patients developed purulent foci elsewhere, such as in a joint, the pericardium, or even in the soft tissues. Presumably, these represent the metastatic lesion of an infected embolus and should alert the physician to a silent lesion of the endocardium. A few patients actually recover from the meningitis only to succumb to the toxemia of the underlying disease or to a cardiac complication.

Of the accessory examinations, blood culture is probably the most important. It is very difficult to sustain the diagnosis of pneumococcal endocarditis without culturing the pneumococcus from the blood stream; the organism grows readily in broth cultures, and cultures should be taken at frequent intervals for prognostic as well as diagnostic purposes. There is almost always an associated leukocytosis characteristic of pneumococcal infections; counts of 50,000 leukocytes have been noted, but the median count probably lies in the neighborhood of 20,000 to 25,000 with a corresponding increase in the band form of neutrophils. There is frequently a hypochromic anemia, sometimes even requiring transfusion.

Examination of the urine is rarely of diagnostic value. Albuminuria may be noted frequently but not in unusual amounts. In a few cases, hematuria may reflect embolic phenomena from the endocardial lesions.

Rarely does the electrocardiogram disclose evidence of diagnostic value in pneumococcal endocarditis.

The course of patients with pneumococcal endocarditis is usually one leading to a rapidly fatal outcome. These patients usually become increasingly toxic and succumb either to toxemia or meningitis. Some expire because of cardiac failure, secondary to deformity or rupture of a valve cusp. The duration of the disease varies considerably even in the untreated patients. It is difficult to ascertain the precise onset of the endocarditis, especially in patients whose endocardial lesion merges with the primary pulmonary disease. As a rule, these patients do not survive longer than 6 weeks; notable exceptions to this survival period have been reported. In a case report of 1943,[8] the patient was known to have had recurring pneumococcemia for at least 172 days; an antemortem diagnosis of endocarditis had been made largely by exclusion but could not be substantiated by physical signs, and no primary focus could be disclosed by history or by culture of various fluids.

It may be seen from the foregoing composite history of cases of pneumococcal endocarditis that often there are no signs or symptoms which characterize the disease clinically. Hence, it is necessary to attempt to confirm even one's suspicion with blood cultures. Demonstration of the pneumococcus by blood culture alone may suggest the diagnosis or confirm a suspicion of endocarditis. Repeatedly positive blood cultures are presumptive evidence of the disease. Rarely has a case of pneumococcal endocarditis been reported at necropsy when antemortem blood cultures in suitable media were negative. The development of embolic lesions during the course of a pneumococcemic infection should be considered suspicious evidence of an endocardial complication. The actual diagnosis of the site of the complication by physical or auscultatory findings may elude detection entirely. The most commonly observed sign permitting the anatomic diagnosis antemortem has been the murmur of aortic insufficiency and associated pulse signs characteristic of incompetence of the aortic valve. Rarely did a systolic murmur or even a change in the character of a systolic murmur in this series of cases enable the physician to localize the lesion with the certitude which the development of an aortic diastolic murmur adds to the diagnostic possibilities. In one well-recorded case, Scott[9] reported the development of a murmur characteristic of mitral stenosis; at necropsy the vegetations on the mitral valve cusps partially occluded the orifice of this valve.

In summary, therefore, it may be said that the diagnosis of pneumococcal endocarditis must be based primarily on a high degree of suspicion. The persistence of pneumococcemia, or the recurrence of a positive blood culture of the pneumococcus, in a patient receiving antimicrobial therapy directed at this organism should alert the physician to the possibility that endocarditis may be

TABLE IV. SUMMARY OF REPORTED CURES OF PNEUMOCOCCAL ENDOCARDITIS

REFERENCE	YEAR OF REPORT	AGE OF PATIENT	TYPE	IMPORTANT THERAPEUTIC AGENTS
13	1902	68	Untyped	Serum
12	1904	25	Untyped	
		18	Untyped	
11	1928	56	Untyped	Serum, vaccine, abscess of fixation
16	1942	18	XXVIII	Serum, sulfadiazine, sulfathiazole
17	1943	—	Untyped	Penicillin
14	1944	7	XXVII	Sulfadiazine, penicillin
18	1945	35	VII	Sulfadiazine, penicillin
		62	V	Sulfadiazine, penicillin
19	1945	1	XIV	Penicillin
20	1946	22	Untyped	Penicillin
7	1946	10	I	Penicillin, then ligation of ductus
21	1946	62	I	Penicillin
22	1946	20	Untyped	Sulfadiazine
23	1947	13	V	Penicillin
24	1950	19	Untyped	Penicillin, sulfadiazine
		25	Untyped	Penicillin, sulfadiazine
25	1951	58	XX	Aureomycin, penicillin
10	1957	44	VIII	Penicillin
		55	XVIII	Penicillin
		40	III	Penicillin

present. If laboratory facilities are available which detect not only the pneumococcus but, also, simultaneous circulating type-specific antibodies, the suspicion should certainly be increased; this is especially true when no other pyemic focus can be ascertained. Moreover, if embolic phenomena occur in the course of the patient's illness, the likelihood of endocarditis is increased. When heart murmurs develop or change in intensity, especially those heard in diastole, these can usually be ascribed to endocarditis in the face of a persisting pneumococcemia.

As noted at the outset, pneumococcal endocarditis was almost invariably fatal even when large doses of type-specific anti-pneumococcus serum were administered relatively early in the course of the disease. Whether there is a failure of the phagocytosis mechanism, an issue raised by Austrian,[10] cannot be answered at this time. At any rate, prevention should be the goal of the therapist, for even today the treatment of this complication of pneumococcal infections is not satisfactory.

In the era before the sulfonamides three case reports appeared indicating that patients recovered from illnesses in which endocarditis developed during the course of an acute pneumococcal infection. Lanbry and Coffin[11] reported the recovery of a Type-II patient after serum, vaccine, and nonspecific therapy. Preble[12] reported 2 young patients who recovered, but he did not comment on the therapy employed. The case report of Wells[13] seems less reliable, for the blood cultures were repeatedly sterile and the hectic course of the patient's convalescence may well have been due to serum sickness.

The widespread use of the sulfonamides has undoubtedly reduced the mortality from pneumococcal pneumonia appreciably, but there is no evidence that the use of these agents is of much value in the treatment of pneumococcal endocarditis. On the other hand, penicillin seems to have exercised a favorable effect on 15 of the patients who have been reported as survivors of this complication. It is impossible to extract a recommended dose of penicillin from these case reports; in view of the disappointing results usually seen, it would seem wise to err on the side of overtreatment rather than to interrupt antibiotic therapy prematurely; fever and blood cultures might serve as parallel indices of adequacy of therapy. While Loewe and associates[14] first recommended combining heparin with penicillin, it is doubtful whether there is need for such adjunctive therapy now. Of course, if there is a lesion amenable to surgical therapy, as in the case reported by Flett and Powell,[7] it would seem wise to subject the patient to an excision of the focal lesion, if, as, and when the patient's general condition permits.

Other temporary cures of pneumococcal endocarditis have been observed, only to have the patient die of a ruptured valve cusp or cardiac failure secondary to a deformed valve.[10] Although the number of cases is still too small for generalization, it does appear that penicillin is superior to the broad spectrum antibiotics in its ability to sterilize the lesions of pneumococcal endocarditis. Sheldon and Golden[15] have pointed out the frequent finding of abscesses of the valve rings in patients with acute bacterial endocarditis who had been treated with antibiotics. The reason for the clearing of the endocardial lesion and the inability of the antibiotic to assist in clearing the abscess is not clear but may represent a failure of the phagocytic mechanism, as Austrian suggests.[10]

It appears from an inspection of these cures that one type of pneumococcus is no more or no less amenable to therapy than another. Likewise, it seems certain that endocardial complications of pneumococcal infections are difficult to treat satisfactorily. Consequently, the therapy of such infections should be aimed at the primary infection, with a view to the prevention of complications of all kinds. Therefore, no attempt has been made to delineate the general or specific measures for the treatment of pneumococcal infections.

SUMMARY

Pneumococcal endocarditis remains a complication of very serious prognostic import. Inasmuch as it may occur in patients with previously undamaged valves, every pneumococcal infection should be treated vigorously and early, with the aim of preventing endocardial complications.

The diagnosis of pneumococcal endocarditis should be suspected in any pneumococcal infection associated with persistent or recurring pneumococcemia. The occurrence of embolic phenomena or meningitis in such infections should add to the suspicion and demand careful examination of the heart. The appearance of a systolic murmur or the roughening of a pre-existing systolic murmur in a patient with pneumococcemia should be regarded as presumptive evidence of endocarditis. A diastolic murmur, especially over the aortic valvular area, appearing in the course of pneumococcemic disease is almost positive proof of endocarditis due to the pneumococcus.

The therapy of pneumococcal endocarditis is unsatisfactory and disappointing, but these patients should be given the benefit of large parenteral doses of penicillin for extended periods after the subsidence of fever, and the sterilization of the blood stream as adjudged by frequent blood cultures.

REFERENCES

1. Perry, C. B.: Bacterial Endocarditis, Bristol, 1936, John Wright & Sons, Ltd.
2. Keefer, C. S.: Am. Heart J. **19**:352, 1940.
3. Bullowa, J. G. M., and Wilcox, C.: Arch. Int. Med. **55**:558, 1935.
4. Wadsworth, A. B.: J. Med. Res. **39**:279, 1918.
5. Allen, A. C.: Arch. Path. **27**:399, 1939.
6. Goldburgh, L. H., Baer, S., and Lieber, M. M.: Am. J. M. Sc. **204**:319, 1942.
7. Flett, D. N., and Powell, W. N.: J.A.M.A. **131**:397, 1946.
8. Ruegsegger, J. M.: Ohio State M. J. **39**:117, 1943.
9. Scott, T.: Internat. Clin. **2**:225, 1941.
10. Austrian, R.: Arch. Int. Med. **99**:539, 1957.
11. Lanbry, C., and Coffin, M.: Bull. et mém. Soc. méd. hôp. Paris **52**:281, 1928.
12. Preble, H. B.: Am. J. M. Sc. **128**:782, 1904.
13. Wells, E. F.: J.A.M.A. **39**:978, 1902.
14. Loewe, L., Rosenblatt, P., Greene, H. J., and Russell, M.: J.A.M.A. **124**:144, 1944.
15. Sheldon, W. H., and Golden, A.: Circulation **4**:1, 1951.
16. Blumberg, N., Heine, W., and Lipshutz, J.: J.A.M.A. **120**:607, 1942.
17. Keefer, C. S., Blake, F. G., Kennerly, M., Jr., Lockwood, J. S., and Wood, W. B., Jr.: J.A.M.A. **122**:1217, 1943.
18. Meads, M., Harris, H. W., and Finland, M.: New England J. Med. **232**:463, 1945.
19. Kugelmass, I. N.: New York State J. Med. **45**:1460, 1945.
20. Lutembacher, R.: Bull. méd., Paris **60**:30, 1946.
21. Favour, C. B., Janeway, C. A., Gibson, J. G., and Levine, S. A.: New England J. Med. **234**:71, 1946.
22. Allesandri R., H., Soza W., M., Pliscoff, G. R., and Diaz Currasco, E.: Rev. méd. Chile **74**:60, 1946.

23. Thill, T. J., and Meyer, O. O.: Am. J. M. Sc. **213**:300, 1947.
24. Orgain, E. S., and Donegan, C. K.: Ann. Int. Med. **32**:1099, 1950.
25. Spies, H. W., Dowling, H. F., Lepper, M. W., Wolfe, C. K., and Caldwell, E. R., Jr.: Arch. Int. Med. **87**:66, 1951.
26. Lacorte, J. G., and Santos, M.: Acta med., Rio de Janeiro **7**:109, 1941.
27. Cullinan, E. R., and Baxter, W. S.: Am. Heart J. **6**:420, 1931.
28. Rakov, H. L.: Am. Heart J. **18**:500, 1939.
29. Lisa, J. R., and Solomon, C.: Am. Heart J. **23**:197, 1942.
30. Koletsky, S.: Am. Heart J. **23**:208, 1942.
31. Zeman, F. D., and Siegal, S.: Am. Heart J. **29**:597, 1945.
32. Geiger, A. J., and Anderson, H. C.: Am. Heart J. **33**:240, 1947.
33. Pray, L. G.: Am. J. Dis. Child. **62**:295, 1941.
34. Stanley, M. M.: Am. J. Med. **2**:253, 1947.
35. Sicard, M. H.: Am. J. M. Sc. **128**:797, 1904.
36. St. George, A. V.: Am. J. M. Sc. **162**:556, 1921.
37. Johnston, J. I., and Johnston, J. M.: Am. J. M. Sc. **177**:843, 1929.
38. Wilkins, R. W., and Weiss, S.: Am. J. M. Sc. **194**:199, 1937.
39. Terry, L. L., and Beard, E. E.: Am. J. M. Sc. **199**:63, 1940.
40. Goldburgh, H. L., Baer, S., and Lieber, M. M.: Am. J. M. Sc. **204**:319, 1942.
41. Flippin, H. F., Gefter, W. I., Domm, A. H., and Clark, J. H.: Am. J. M. Sc. **206**:216, 1943.
42. Marr, H. R., and Hecht, E. L.: Am. J. Surg. **161**:150, 1943.
43. Alpert, S., and Gottlieb, C.: Am. Rev. Tuberc. **42**:807, 1940.
44. Feissinger, N., and Arnaudet, A.: Ann. d'anat. path., Paris **9**:213, 1932.
45. Finland, M.: Ann. Int. Med. **10**:1531, 1937.
46. Blake, F. G.: Ann. Int. Med. **5**:673, 1931.
47. Toone, E. C.: Ann. Int. Med. **14**:1551, 1941.
48. Heyer, H. E., and Hick, F. K.: Ann. Int. Med. **15**:291, 1941.
49. Wilhelm, F., Hirsh, H. L., Hussey, H. H., and Dowling, H. F.: Ann. Int. Med. **26**:221, 1947.
50. Lapage, C. P., and Langley, F. A.: Arch. Dis. Childhood **22**:253, 1947.
51. Cecil, R. L., Baldwin, H. S., and Larsen, N. P.: Arch. Int. Med. **40**:253, 1927.
52. Braunstein, A. L., and Townsend, S. R.: Arch. Int. Med. **65**:957, 1940.
53. Garvin, C. F.: Arch. Int. Med. **66**:1246, 1940.
54. Moore, F. J., Thomas, R. E., Kistler, M., Ireland, R. M., and Hallstone, V. E.: Arch. Int. Med. **66**:1290, 1940.
55. Price, A. E., and Myers, G. B.: Arch. Int. Med. **70**:558, 1942.
56. Tinsley, C. M.: Arch. Int. Med. **75**:82, 1945.
57. Feissinger, N., and Roudowska, L.: Arch. mal. coeur **5**:97, 1912.
58. Lutembacher, R., and Butillon, F.: Arch. mal. coeur **18**:145, 1925.
59. Silverman, D., and Turner, M.: Arch. Otolaryng. **30**:431, 1939.
60. Cabezas, A.: Arch. Col. méd. El Salvador **1**:323, 1948.
61. Dean, H. R.: Brit. J. Child. Dis. **9**:317, 1912.
62. Lumsden, J.: Brit. M. J. **1**:890, 1921.
63. Tattersall, R. N.: Brit. M. J. **1**:293, 1942.
64. Bloomfield, A.: Bull. Johns Hopkins Hosp. **28**:301, 1917.
65. Thomas, H. M., and O'Hara, D.: Bull. Johns Hopkins Hosp. **31**:417, 1920.
66. Meuetrier, P.: Bull. et mém. Soc. méd. hôp., Paris **48**:679, 1919.
67. Lenoble, M. E., and Labellec, M.: Bull. et mém. Soc. méd. hôp., Paris **47**:1256, 1923.
68. Merklen, P., and Wolf, M.: Bull. et mém. Soc. méd. hôp., Paris **48**:718, 1924.
69. Netter, A., and Salanier, M.: Bull. et mém. Soc. méd. hôp., Paris **52**:275, 1928.
70. Lanbry, C., and Coffin, M.: Bull. et mém. Soc. méd. hôp., Paris **52**:281, 1928.
71. Boiden, M. L., Mme. Bertrand-Fontaine, and Mlle. Fayot: Bull. et mém. Soc. méd. hôp., Paris **54**:1242, 1930.
72. Pichon, E., and Pham-lu-chi: Bull. et mém. Soc. méd. hôp., Paris **49**:355, 1933.
73. Plazy, J. M., and Damany, C.: Bull. et mém. Soc. méd. hôp., Paris **49**:879, 1933.
74. Huber, J., Lievre, J. A., and Paget, M.: Bull. et mém. Soc. méd. hôp., Paris **55**:181, 1939.
75. Griffon, V.: Bull. Soc. anat., Paris **72**:622, 1897.
76. Novak, E.: Bull. Univ. Maryland School of Med. **13**:209, 1929.
77. Kennedy, W. R.: Canad. M. A. J. **19**:336, 1928.
78. Gydesen, C. S.: Colorado Med. **28**:74, 1931.
79. Thayer, W. S.: Edinburgh M. J. **38**:307, 1931.
80. Bureau, M.: La France méd. **32**:177, 1892.
81. Traut, E. F., Carter, J. B., Gumbiner, S. H., and Hench, R. N.: Geriatrics **4**:205, 1949.
82. Venchiuretti, P.: Gior. veneto di sc. med. **13**:471, 1939.
83. Fishkin, B. G., and Pilot, I.: Illinois M. J. **77**:244, 1940.
84. Apfelbach, C. W.: Illinois M. J. **81**:158, 1942.
85. Lemann, I. I.: Internat. Clin. **2**:66, 1931.
86. Goldstein, H. I., Goldstein, H. Z.: Internat. Clin. **3**:155, 1927.

87. Pollock, J. H.: Irish M. J. **5**:18, 1923.
88. Kapsinorv, R.: J.A.M.A. **95**:409, 1930.
89. Cecil, R. L., and Plummer, N.: J.A.M.A. **98**:779, 1932.
90. Rhoads, P. S., Hoyne, A. L., Levin, B., Horswell, R. G., Reals, W. H., and Fox, W. W.: J.A.M.A. **115**:917, 1940.
91. Dawson, M. H., and Hobby, G. L.: J.A.M.A. **124**:611, 1944.
92. Bruno, M. S., and Hochstein, E.: J.A.M.A. **148**:93, 1952.
93. Hollander, A., and Landsberg, E.: J. Lab. & Clin. Med. **26**:307, 1940.
94. Trasoff, A., and Meranze, D. R.: J. Lab. & Clin. Med. **29**:590, 1944.
95. Steele, C. W., and Gottlieb, J.: J. Maine M. A. **35**:81, 1944.
96. Creyx, M., Damade, R., and Massias, C.: J. méd., Bordeaux **94**:168, 1922.
97. Wood, W. B., Jr., and Moore, R. A.: J. Missouri M. A. **40**:319, 1943.
98. Cooke, W. T.: Lancet **2**:510, 1941.
99. McCartney, D. W., Luxton, R. W., Smith, G. S., Ramsay, W. A., and Goldman, J.: Lancet **1**:639, 1942.
100. Rosenblüth, M. B.: Litman Ann. **3**:983, 1932.
101. Palmer, W. W.: M. Clin. North America **2**:987, 1919.
102. Funk, E. H.: M. Clin. North America **10**:79, 1926.
103. Bunim, J. J.: M. Clin. North America **30**:584, 1946.
104. Lacorte, J. G., and Santos, M.: Mem. Inst. Oswaldo Cruz **41**:101, 1944.
105. Gamma, C.: Minerva med. **26**:873, 1935.
106. Hall, W. H., Alden, J., Burt, G. M., and Spink, W. W.: Minnesota Med. **29**:553, 1946.
107. Cabot Case No. 20462: New England J. Med. **211**:938, 1934.
108. Locke, E.: New England J. Med. **191**:913, 1924.
109. Thord, F.: New England J. Med. **207**:767, 1932.
110. Finland, M., Brown, J. W., and Rauh, A. E.: New England J. Med. **218**:1033, 1938.
111. Cabot Case #26242: New England J. Med. **222**:1016, 1940.
112. Cabot Case #27522: New England J. Med. **225**:1026, 1941.
113. Cabot Case #28231: New England J. Med. **226**:923, 1942.
114. Cabot Case #28532: New England J. Med. **227**:1047, 1943.
115. Cabot Case #30102: New England J. Med. **230**:293, 1944.
116. Cabot Case #31252: New England J. Med. **232**:739, 1945.
117. Van Metre, T. E., Jr.: New England J. Med. **251**:1048, 1954.
118. Case Report: New York State J. Med. **42**:1765, 1942.
119. Toomey, J. A., and Roach, F. E.: Ohio State M. J. **35**:841, 1939.
120. Lutembacher, R.: Paris méd. **11**:85, 1921.
121. Lewkowicz, K.: Polska gaz. lek. **11**:405, 1932.
122. James, W. B.: Presbyterian Hosp. Rpts. **3**:325, 1898.
123. Tapie, J., and Rouquet, A.: Progrès méd. **35**:403, 1920.
124. Luxton, R. W., and Smith, G. S.: Quart. J. Med. **12**:61, 1943.
125. Cutaldi, G.: Rassegna Internaz. di Clin. e Terap. **14**:630, 1933.
126. Rosselot, J., and Manterola, A.: Rev. Chileña de Pediatria **19**:381, 1948.
127. Cinca, M., Alexa, I., and Agapi, C.: Rev. Stünt. Med. **18**:24, 1929.
128. Gavazzi, N.: Rinasc. med. **9**:80, 1932.
129. Ramos, J.: São Paulo Med. **2**:673, 1932.
130. Tesi, A.: Sett. med. **34**:80, 1946.
131. Karotkin, L., and Marcuse, P.: South. M. J. **39**:769, 1946.
132. Levi, M.: Sperimentale, Arch. di Biol. **87**:609, 1933.
133. Lassen, H. C. A.: Ugeskrift for Laeger **101**:99, 1939.

Coronary Embolism: Report of Three Cases

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INTRODUCTION

Embolism is an uncommon but often fatal type of occlusion of a coronary artery. In a recent collective review,[1] 54 cases of coronary embolism documented by detailed clinical and post-mortem studies were described. The basis for the most common type of embolism, that is, bacterial endocarditis, is not observed as often today as it was formerly. Thrombi of vascular origin were a common source of coronary arterial emboli, and although some success has been achieved in the control of thrombosis and its complications through the use of anticoagulants, such an origin must still be considered. Atheromatous deposits in the sinuses of Valsalva and the proximal aorta may also enter the coronary arterial circulation and result in occlusion more frequently than is presently appreciated. In the three cases to be described, all encountered recently, each of the three mechanisms of embolism of the coronary arteries just described is exemplified. In one, the embolus arose from a vegetation of bacterial endocarditis, in another, from a thrombus in the left atrium, and in the third, from atheromatous deposits in the proximal aorta. In all three cases, death resulted from myocardial infarction.

CASE REPORTS

CASE 1 (P.B.B.H., A-57-364).—J. B. was a 63-year-old, white machinist who had had "rheumatism" at age 17 and an episode of "rheumatoid arthritis" at age 48. He was well until three and one-half years prior to death, at which time he noted the onset of progressive exertional dyspnea, orthopnea, and attacks of wheezing. One and one-half years prior to death he complained of weakness and subxiphoid pain at work, was found to have rheumatic heart disease and atrial fibrillation, and was digitalized. During the year prior to death he lost 30 pounds, had a chronic cough with occasional hemoptysis, and became more orthopneic. Twenty-four days prior to death he had an acute attack of substernal pain with increased dyspnea. The following day he had three generalized convulsive seizures and an episode of apnea. He then entered the hospital with severe parieto-occipital headaches, confusion, and disorientation.

Physical Examination.—Physical examination on admission showed a small, dyspneic, and orthopneic man who coughed occasionally, each cough apparently precipitating a severe parieto-occipital headache. His blood pressure was 90/60 mm. Hg, pulse 100, and respirations 20. The only pulmonary findings were breath sounds which had a prolonged and high-pitched expiratory

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phase. The neck veins were not distended and there was no cyanosis. There was a marked precordial heave and an epigastric impulse. The heart sounds were distant, M_1 was greater than M_2, and there was a Grade 1 apical, medium-pitched systolic murmur. No evidence of diastolic murmur, gallop, rub, or thrill was found. Admission ECG showed atrial fibrillation, digitalis effect, and abnormal nonspecific S-T segment changes in the precordial leads. Venous pressure was 210 mm. Hg, and circulation time (arm to tongue) was 32 seconds. The transaminase was 210 units on admission and fell to 25 units nine days later.

Shortly after admission the patient developed a pericardial friction rub and S-T segment depressions over the lateral precordial leads (Fig. 1); together with the elevated transaminase this established the diagnosis of myocardial infarction. Twenty days prior to death he had had an episode of hematemesis and guaiac-positive stools. Dyspnea and low-grade fever persisted, and on the sixteenth day prior to death he showed the signs of a pneumonic process in the right middle and lower lobes. Because of the failure of this process to respond to penicillin and streptomycin, recurrent pulmonary emboli were suspected, and both femoral veins were ligated under local anesthesia twelve days prior to death. The patient failed to respond to this procedure and went steadily downhill, with the blood urea nitrogen rising from 20 to 110 mg. per cent and potassium rising from 4.4 to 7.2 mEq./L. Over the last ten days of life a progressively louder apical diastolic murmur appeared which had some of the qualities of a mitral stenosis rumble. The pulmonary involvement became more extensive, and the patient died quietly on the morning of the twenty-fourth hospital day.

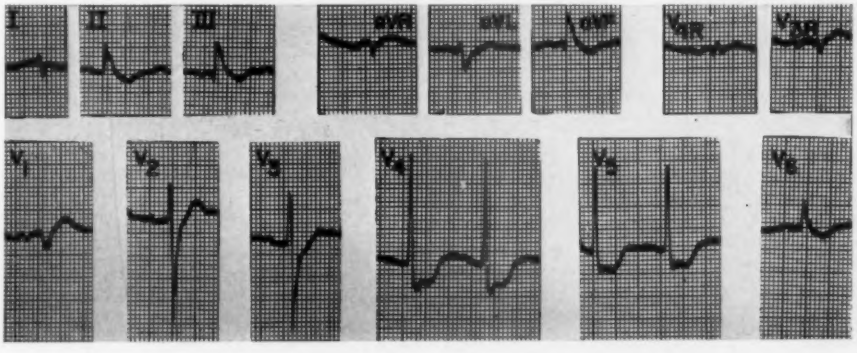

Fig. 1.—Case 1. ECG showing depression of the S-T segment.

Autopsy.—At autopsy, mitral stenosis was demonstrable, with a posterior wall and septal myocardial infarction caused by embolic occlusion of the circumflex branch of the left coronary artery which supplied most of the posterior left ventricle and septum (Fig. 2). The coronary vessels had only minimal atherosclerosis, and did not contribute to the occlusion. Histologic dating placed the infarct at three to four weeks old (Fig. 3). The source of the embolus was a mural thrombus on the left atrial wall. The major portion represented a recent process, perhaps three to four days old, and thus not old enough to have been that portion which produced the occlusion. Its site of attachment, however, was organized and approximately three to four weeks old, as was the embolus (Figs. 4 and 5). Thus, the site of attachment was part of an older process which gave off the fatal embolus, after which the recent thrombus had formed on it. There was no rupture of a papillary muscle and no ulceration or other recent defects of the cardiac valves. There was evidence of an active rheumatic process with fibrinoid, Aschoff cells, and fibrinous pericarditis.

There was hemorrhagic consolidation of the lower lobes of the lungs. The organized thrombi in the small arteries, partially organized masses of fibrin in the alveoli, and capillary fibrin plugs were all consistent with a recurrent embolic process extending over a period of several weeks.

A subacute peptic ulcer found on the lesser curvature of the stomach was the most likely source of the guaiac-positive stools and hematemesis.

The rise in blood urea nitrogen could not be explained on an anatomic basis. The most plausible postulate would be prerenal azotemia secondary to congestive heart failure, bleeding from the peptic ulcer, and decreased glomerular filtration rate.

Fig. 2.—Case 1. Embolus lodged in the circumflex branch of the left coronary artery.

Fig. 3.—Case 1. Myocardial infarction showing organization by vascular fibrous tissue. Hematoxylin and eosin, 4 micron section. Original magnification, × 90.

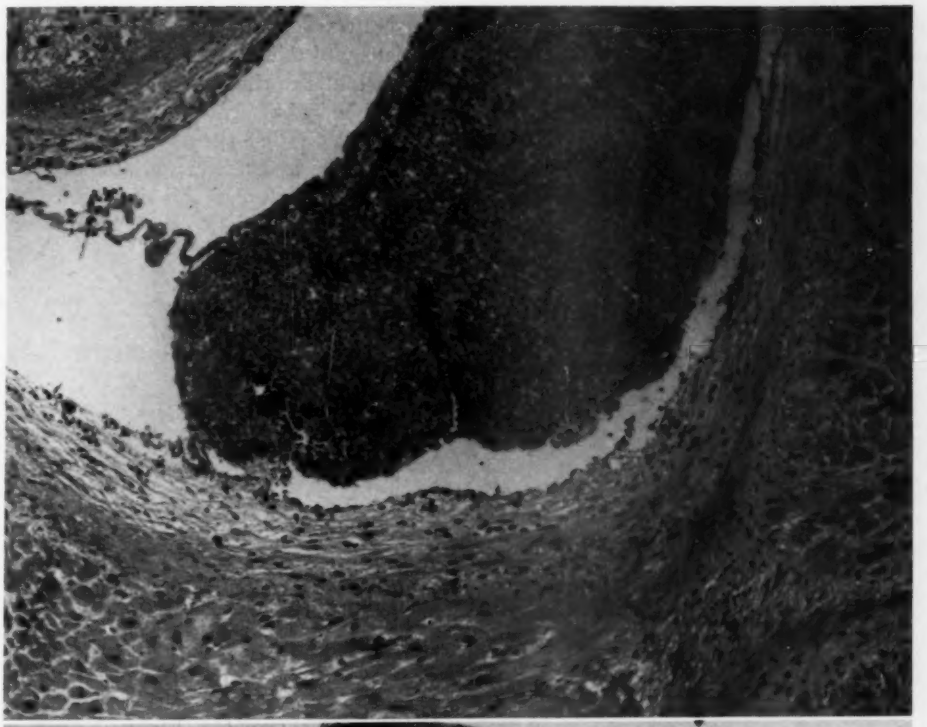

Fig. 4.

Fig. 5.

Fig. 4.—Case 1. Thrombus in the left atrium, showing attachment to the wall. Hematoxylin and eosin, 4 micron section. Original magnification, × 90.

Fig. 5.—Case 1. Embolus from the circumflex branch of the left coronary artery. Trichrome, 4 micron section. Original magnification, × 90.

CASE 2 (W.R.V.A.H., A57-43).—P. S. was a 34-year-old white man who was known to have had a heart murmur since birth. There was no known history of rheumatic fever, scarlet fever, or cyanosis, but an apparently significant murmur was heard at the time of discharge from the Armed Forces in 1946. He did well until March of 1953, when he had an episode suggesting paroxysmal tachycardia. At this time his family physician reported a Grade 3 systolic murmur radiating over the entire precordium, being maximal at the left of the lower sternum, and the ECG demonstrated left and right ventricular hypertrophy. The blood pressure at this time was 140/30 mm. Hg. In June of 1955, a diastolic murmur was heard at the left sternal border. Two months

Fig. 6.—Case 2. *A*, Vegetative endocarditis of the mitral valve. *B*, Vegetative endocarditis of the aortic valve. Note destructive lesion in cusp on right.

prior to admission he developed generalized aches, malaise, fever, sweats and chills; there was no history of dental extractions. Six weeks prior to admission he developed palpitations, a heavy precordial sensation forcing him to sleep in an elevated position, and ankle edema. He was admitted to another hospital where blood cultures were positive for *Streptococcus viridans*, and he was placed on massive doses of penicillin plus 2 Gm. of streptomycin per day. There was a good temperature response to this therapy but tachycardia persisted. He was then admitted to the West Roxbury Veterans Administration Hospital for further therapy of bacterial endocarditis.

Physical Examination.—The patient was well developed and well nourished, with a blood pressure of 134/0 mm. Hg, pulse of 112, and temperature of 98.6° F. The neck veins were flat. There were decreased breath sounds at the bases bilaterally, and no râles were heard. The heart was slightly enlarged to the left; A_2 was absent; and a Grade 4, harsh systolic murmur and thrill

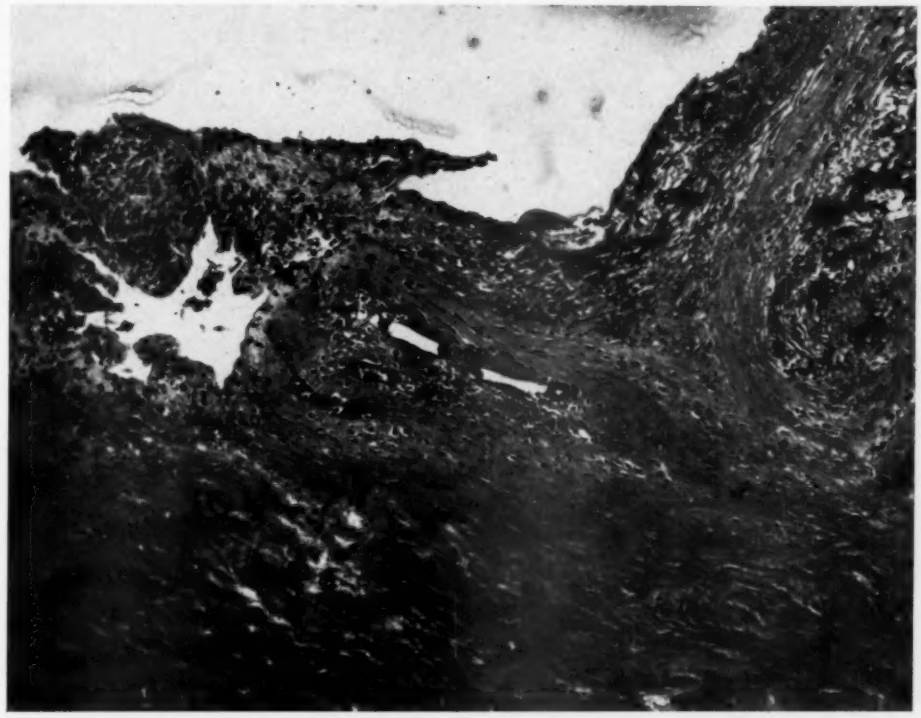

Fig. 7.—Case 2. Section of the aortic valve, showing the vegetative endocarditis. Hematoxylin and eosin, 4 micron section. Original magnification, × 90.

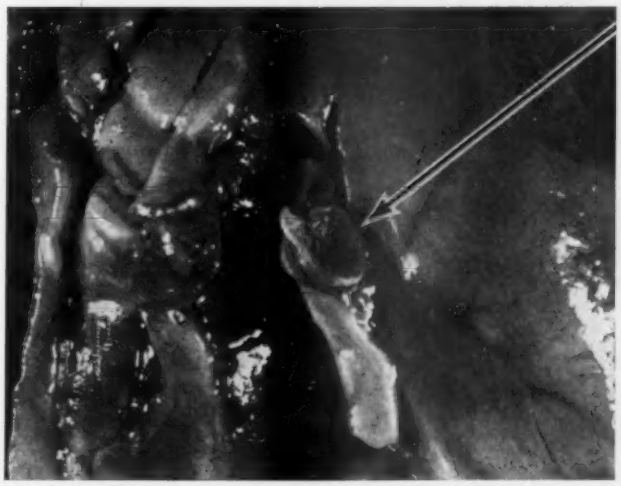

Fig. 8.—Case 2. Embolus with mycotic aneurysm formation in the obtuse branch of the left circumflex coronary artery. Arrow points to cut end of artery at the site of occlusion and aneurysm formation.

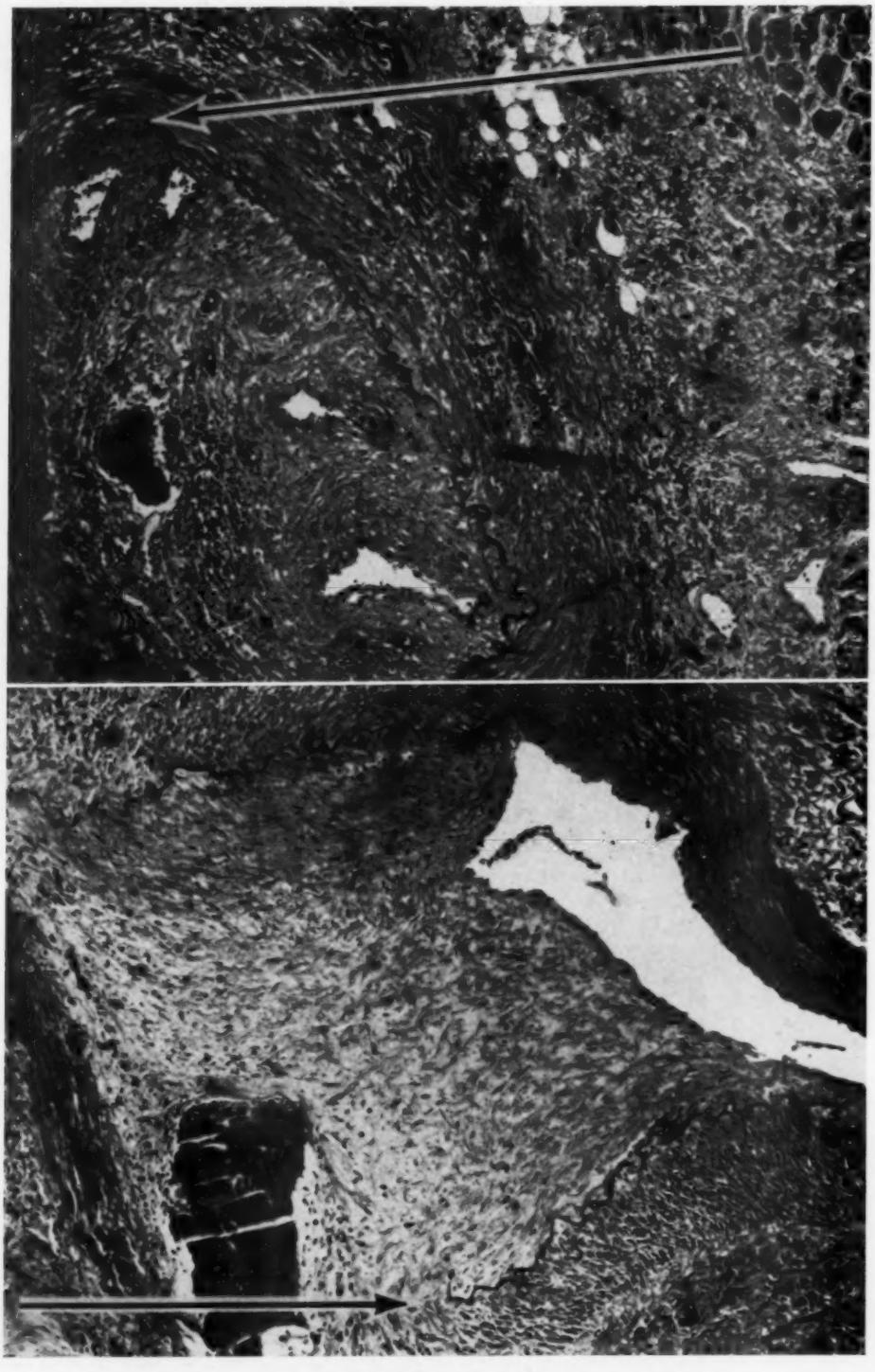

Fig. 9.—Case 2. *A* and *B*, Section of the partially organized embolus in the obtuse branch of the left circumflex coronary artery with adjacent infarct. Note disruption of elastic lamella, with fragmentation and partial disruption of the media (see arrows). Elastic tissue stain, 4 micron section. Original magnification, × 90.

were noted in the left mid-clavicular line in the sixth intercostal space. A diastolic murmur at the left sternal border was also noted, and there was a pistol-shot murmur over the brachial and femoral arteries. The remainder of the findings on physical examination were within normal limits.

Laboratory work on admission revealed a white blood cell count of 9,400, a hemoglobin of 12.8 Gm. per cent, and a hematocrit of 39. The urinalysis was normal. Repeated blood cultures were negative. On admission a chest film showed an enlarged heart with prominence of the left ventricle and diffuse increase in the vascular markings of both lung fields. Cardiac fluoroscopy revealed enlargement of both right and left ventricles and no evidence of valvular calcifications. By ECG there was left ventricular hypertrophy with probable incomplete right bundle branch block, and a bigeminal rhythm.

There was a low-grade fever during the first few days of hospitalization, but following this he remained afebrile. He was relatively asymptomatic except for occasional episodes of anxiety and palpitations. The same dosage of penicillin was continued for nineteen days after admission. A few episodes of cardiac failure were easily controlled by use of sodium restriction and digitalis. Thirty-seven days after admission, while walking down the corridor, he suddenly slumped to the floor and succumbed in spite of resuscitative measures.

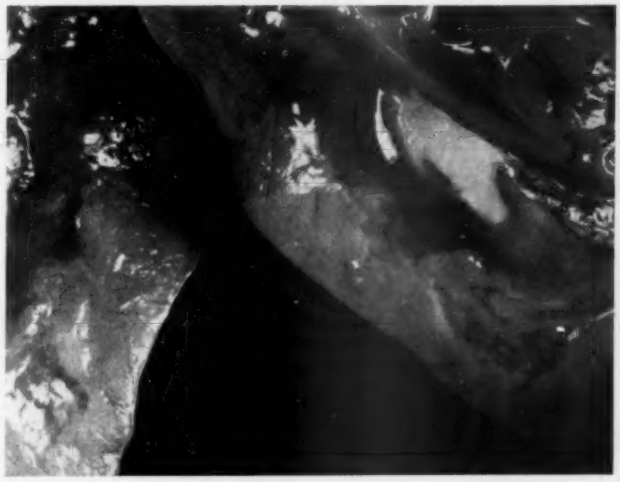

Fig. 10.—Case 2. Infarct of the left ventricle.

Autopsy.—At autopsy the heart weighed 725 grams. A vegetative endocarditis was present on both the aortic and mitral valves (Figs. 6, *A*, *B* and 7). The aortic cusps had thickened and slightly retracted edges. There was slight thickening of the chordae tendineae of the posterior leaflet of the mitral valve, and the anterior leaflet was thickened at its edge and its chordae tendineae were thickened and fused. There was minimal coronary atherosclerosis. A large branch of the left circumflex coronary artery was dilated and completely occluded by a thrombus (Fig. 8). Microscopically, the vessel showed partial destruction of its wall, with granulomatous inflammation about calcified debris, presumably fragments of valve vegetation (Fig. 9, A and *B*). The myocardium of the left posterolateral wall beneath this vessel contained a large focus of recent infarction (Figs. 9, *A* and 10). There were small, partially organized infarcts in the spleen, with small arteries and arterioles occluded by partially organized thrombi.

The destructive process suggests a preceding septic embolus, with resultant myocardial infarction and mycotic aneurysm formation. The microscopic alterations in the mitral and aortic valves suggest rheumatic heart disease as the underlying cardiac disease. The microscopic appearance of the coronary embolus is identical with the vegetative lesion involving the aortic and mitral valves (Fig. 7).

CASE 3 (P.B.B.H., A-58-108).—B. M. was an 87-year-old widower who had been well up to six months prior to death, at which time he developed a cough and mild congestive heart failure. For a week prior to death he had increasing shortness of breath, wheezing, and dyspnea on exertion. On the day before death he complained of anterior chest pain radiating through to the back, with nausea and sweating. He entered the hospital in pulmonary edema.

Physical Examination.—Physical examination on admission showed an elderly, dyspneic white man with cyanotic lips. His blood pressure was 150/100 mm. Hg, pulse 88, and respirations 28. The chest was increased in anteroposterior diameter, the expiratory phase of respiration was prolonged, and there were coarse rhonchi and râles throughout both lung fields. The heart sounds were obscured. The admission ECG showed an anteroseptal myocardial infarct, frequent multifocal ventricular premature beats, often in runs of bigeminy, and occasional nodal premature beats (Fig. 11). The sedimentation rate was 33, the white blood cell count was 8,800 with 89 per cent neutrophils; lactic dehydrogenase was 340 (normal 117 or less); and blood urea nitrogen was 59 mg. per cent.

The patient seemed to be comfortable and to do well on initial therapy, but on the night of admission he had a sudden convulsion and expired.

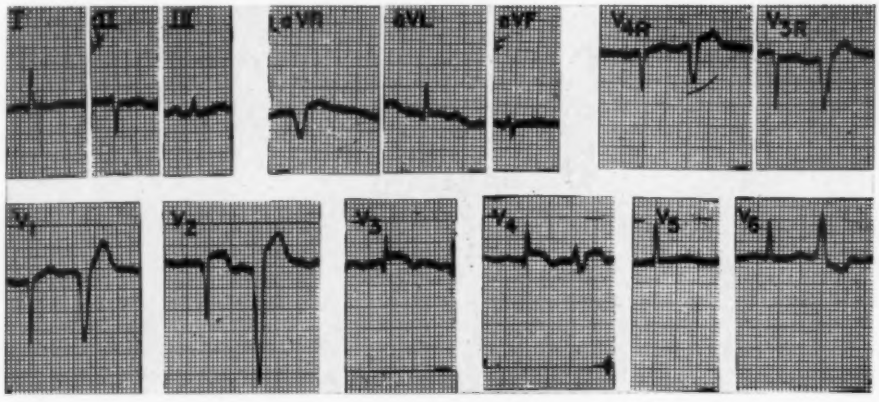

Fig. 11.—Case 3. ECG showing the changes of an anteroseptal myocardial infarction.

Autopsy.—At autopsy there was severe generalized atherosclerosis. The heart weighed 460 grams and had an old, healed septal myocardial infarct and a quite recent myocardial infarction which involved the anterior septum and apex of the left ventricle, and which was histologically dated as less than 24 hours old. The anterior descending branch of the left coronary artery was markedly sclerotic, with the media consisting of dense fibrous tissue and a few scattered bundles of smooth muscle, and the intima consisting of proliferated fibrous tissue containing cholesterol, foci of calcification, hemosiderin-laden macrophages, lymphocytes, and plasma cells. The narrowed lumen contained a recent embolus made up of amorphous, granular, eosinophilic material, cholesterol, and red cells (Fig. 12). There was a neutrophilic inflammatory reaction at the site of attachment of the embolus to the artery wall, which extended into the embolus itself. Above each of the sinuses of Valsalva there were firm excrescences showing focal calcification, cholesterol deposition, and granular debris; however, each was covered by a continuous band of fibrous tissue containing a few elastic fibers. Just above the aortic valve there were several large, ulcerating atheromata. Such atheromata were found throughout the aorta, and just above the bifurcation there was a thrombosed saccular aneurysm. Histologically, the atheromata were composed of the same type of amorphous, granular, eosinophilic material containing cholesterol and some red cells as was the embolus that occluded the anterior branch of the left coronary artery (Fig. 13). The surface of this material was not covered by any fibrous tissue, but rather had such amorphous material projecting freely into the lumen. Above the occlusion there was no evidence of any ulceration in the coronary artery itself that could have acted as a source for the embolus. Additional evidence for the friable atheromata as the source of the coronary embolus was the presence

Fig. 12.

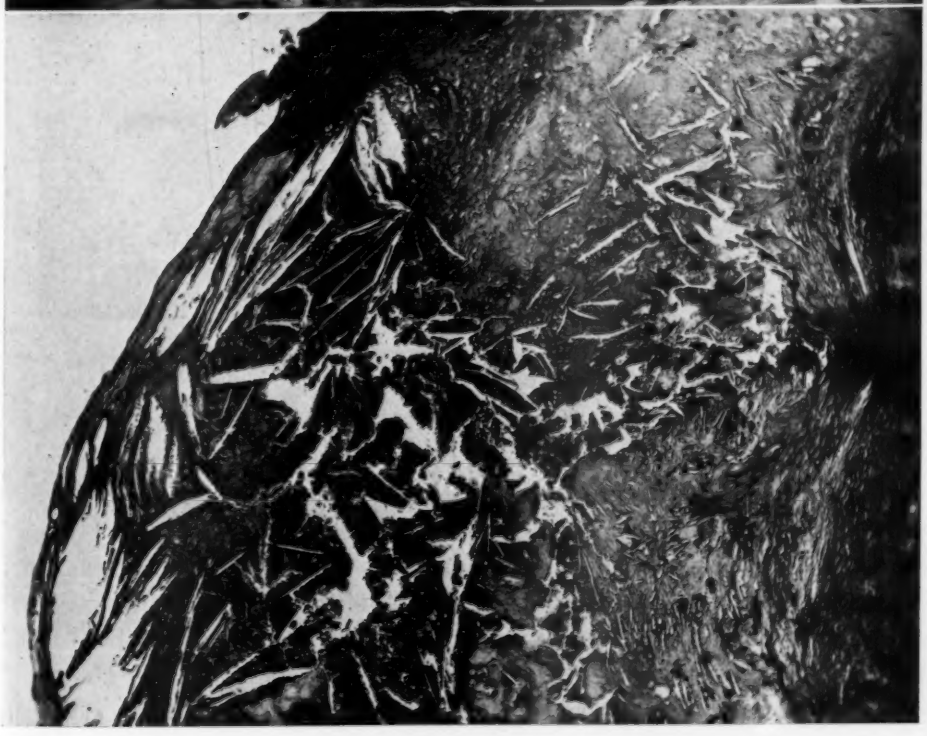

Fig. 13.

Fig. 12.—Case 3. Atheromatous embolus in the anterior descending branch of the left coronary artery, showing its attachment to the wall and infiltration with neutrophils. Hematoxylin and eosin, 4 micron section. Original magnification, × 56.

Fig. 13.—Case 3. Section of an ulcerating atheroma on the aortic wall adjacent to the aortic valve. Hematoxylin and eosin, 4 micron section. Original magnification, × 67.

of atheromatous emboli in the small arteries and arterioles of the spleen, kidneys, periadrenal fat, and pancreas (Fig. 14). The atheromatous embolus must have been carried into the coronary artery from an atheroma near the coronary ostium during the diastolic reflux of blood into the coronary vessels. The kidneys showed severe nephrosclerosis, which was the result of hypertension, and which probably explained the elevated blood urea nitrogen. The lungs were congested and edematous. The immediate cause of death was acute myocardial infarction and subsequent pulmonary edema.

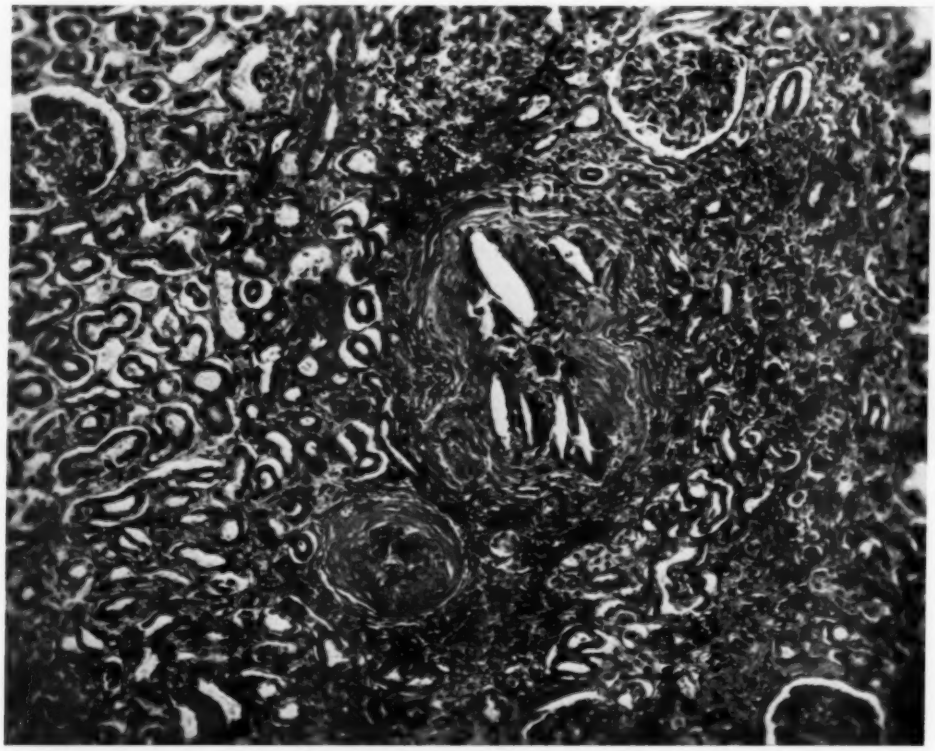

Fig. 14.—Case 3. Atheromatous embolus in a small renal artery. Hematoxylin and eosin, 4 micron section. Original magnification, × 124.

DISCUSSION

In a recent comprehensive review[1] coronary embolism was found to have a 3:1 predominance in males and to occur most frequently between the ages of 20 and 50. The vessel most commonly involved was the left coronary artery, as in all three cases presented here, especially its anterior descending branch. The most common source of emboli was a bacterial vegetation, as in Case 2. The proximal portion of the aorta, as in Case 3, was also frequently the source of emboli. The least common origin of emboli was in the left atrium, where the embolus of Case 1 arose. The over-all mortality from coronary embolism was found to be 96 per cent, but in only 31 per cent was the cause of death ascribed to myocardial infarction. In all three cases reported here, death resulted from myocardial infarction.

Coronary embolism has been reviewed periodically throughout the years,[1-4] and each time relatively few cases have been collected, the last review[1] having only 54 cases. The three cases reported here were observed over a period of approximately four months; thus it seems reasonable to suspect that coronary embolism may be a more common phenomenon than has been appreciated. The demonstration of a coronary embolus requires careful gross and microscopic study, and with such an effort this mechanism of coronary occlusion may well be found more commonly than it has in the past.

SUMMARY

Three cases of coronary embolism resulting in myocardial infarction are reported. The possibility of the more frequent occurrence of this phenomenon in causing myocardial infarction is discussed.

REFERENCES

1. Shrader, E. L., Bawell, M. B., and Moragues, V.: Circulation **14**:1159, 1956.
2. Saphir, O.: Am. Heart J. **8**:312, 1933.
3. Hamman, L.: Am. Heart J. **21**:401, 1941.
4. Moragues, V., Bawell, M. B., and Shrader, E. L.: Circulation **2**:434, 1950.

Marfan's Syndrome: A Case With Complete Dissection of the Aorta

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About 60 autopsied cases of Marfan's syndrome have been reported to date. Eighteen of them had dissecting aneurysm of the aorta.[1,2] Thirty-three cases had aneurysmal dilatation of the ascending aorta. The following case is reported because of some very unusual features found at autopsy.

CASE REPORT

M. J., a 30-year-old, unmarried white woman, entered the Hahnemann Medical College and Hospital on Feb. 6, 1958. Her chief complaints on admission were extreme shortness of breath, cough, and swelling of her face and extremities. The patient did not offer any history of rheumatic fever or its equivalents. She had had cyanosis on exertion since childhood. She was never aware of her heart condition until 1957. At that time a murmur was heard during a physical examination for suspected pneumonia. She also presented evidence of congestive failure. She was put on digitalis medication. Again in January, 1958, she had a severe pneumonitis with evidence of marked congestive failure. She was treated with oxygen, digitalis, antibiotics, and diuretics. Her condition did not improve and she was referred to this hospital for evaluation and treatment. There was nothing noteworthy in the past history except severe myopia since childhood. Family history was noncontributory.

Physical examination revealed a young white woman in acute respiratory distress, with cyanosis of the lips and nail beds. Her supraorbital ridges were prominent. She had a high, narrow, and arched palate. The thoracic cage presented a pigeon-breast deformity with central pectus excavatum. She did not have tall features or long fingers. Pulse rate was 106 per minute and it was regular. Her blood pressure in the upper extremities was 140/0 mm. Hg, and in the lower extremities it was 90/0 mm. Hg. Examination of the eyes revealed nothing abnormal except bulging eyeballs and severe myopia. There was no dislocation of the lens. Neck vessels were pulsating. Lungs were clear. Auscultation of the heart revealed a continuous, systolic-diastolic murmur at the third left intercostal space at the side of the sternum. The same murmur was transmitted over the entire precordium with varying intensity. Abdominal examination revealed the liver to be enlarged 4 fingerbreadths below the right costal margin, and the spleen was enlarged 2 fingerbreadths. Femoral arteries were barely palpable. There was pitting edema in the legs and feet.

The electrocardiogram revealed first degree A-V block and digitalis effect (Fig. 1).

X-ray of the chest revealed a markedly enlarged heart, both to the right and left of the midline. Hilar vessels were obscured by the marked cardiac enlargement. There was a marked anterior deformity of the sternum (Fig. 2).

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The laboratory findings were within normal limits. Blood serology was negative.

At this stage a diagnosis of high ventricular septal defect, deformed aortic valve, and coarctation of the aorta was made.

The patient was treated for congestive failure. However, she developed spiking temperature and some moist râles in the chest. The white blood cell count was 11,700 with 84 per cent polymorphonuclear cells. Urinalysis revealed 2-4 wbc/field. Blood culture was positive for staphylococci coagulase negative on three occasions. The organisms were resistant to all antibiotics except Novobiocin.

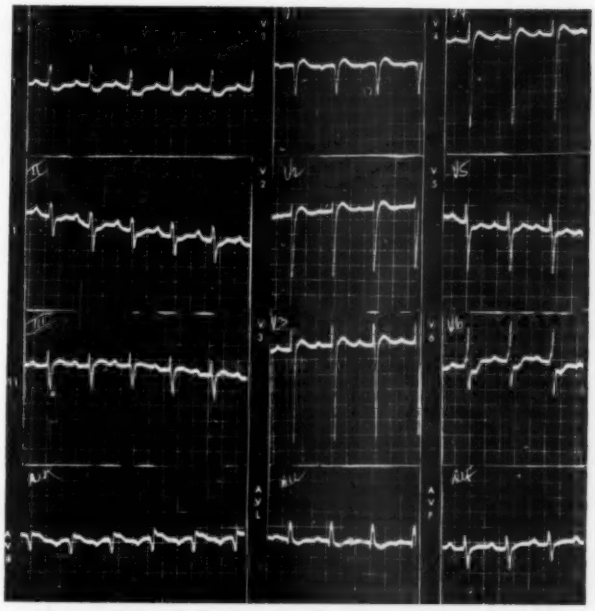

Fig. 1.—Electrocardiogram of the patient, showing first degree A-V block and digitalis effect.

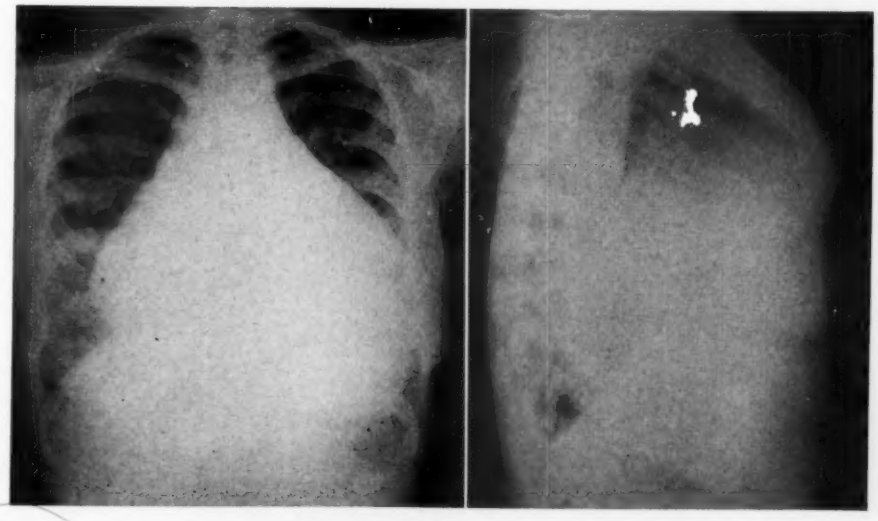

Fig. 2.—Posteroanterior and lateral chest x-ray of the patient, showing markedly enlarged heart and anterior deformity of the sternum.

The clinical course of the patient was progressively downhill. She was treated with heavy doses of penicillin (100 million units intravenously, daily), Achromycin (500 mg. q. 6 h.), Chloromycetin (500 mg. q. 6 h.), Novobiocin (500 mg. q. 6 h.), Spontin (1,500 mg. intravenously b. i. d.), and Vancomycin (1,000 mg. intravenously b.i.d.). In spite of this intensive antibiotic therapy the patient did not show any improvement. She died suddenly on March 8, 1958.

Fig. 3.

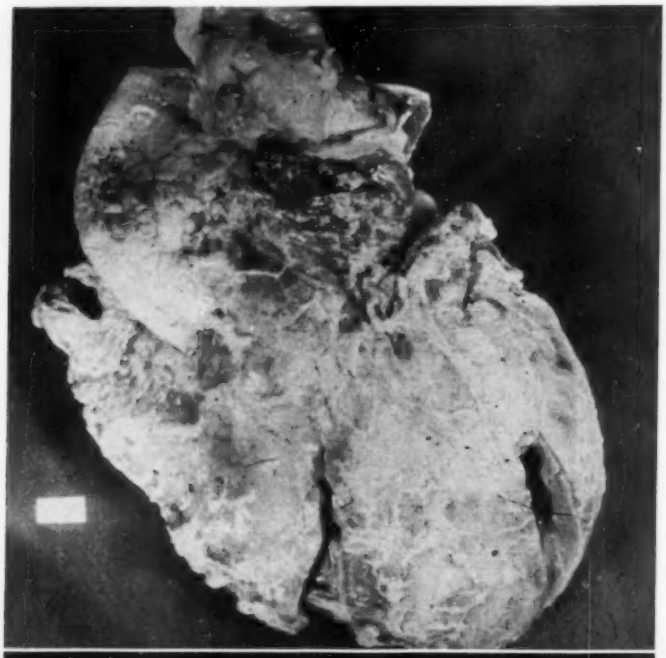

Fig. 4.

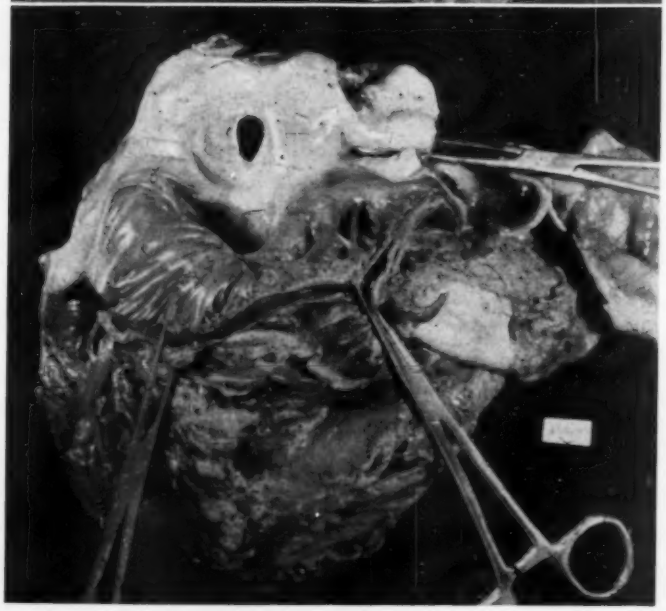

Fig. 3.—Gross specimen of heart showing the rough surface and shaggy coat of fibrin covering the heart.

Fig. 4.—Gross specimen of heart showing the secundum type of atrial septal defect.

Fig. 5.—In this specimen the ascending aorta has been split open to show the normal aortic valves.

Fig. 6.—Ascending aorta has been split open to show the tremendous aneurysm of the ascending aorta. The intima appears ruptured immediately above the cusps and a denudated area covers the media along the circumference.

Fig. 5.

Fig. 6.

Figs. 5 and 6.—*(For legend see opposite page.)*

Autopsy Findings.—

Gross: The heart was very much enlarged. The pericardium had a dull and finely granular surface. It was adherent to the endocardium but could be pulled out leaving a shaggy coat of fibrin covering the heart. There was scattered plastic necrotic exudate in the pericardium (Fig. 3). The endocardium covering both auricles had a gray appearance and was thickened. There was an atrial septal defect of the secundum type, measuring 1.3 cm. in diameter (Fig. 4). The right atrium and right ventricle appeared dilated and hypertrophied. The left ventricle was hypertrophied. All the valves and valve orifices were normal (Fig. 5). There was only one coronary ostium located in the right lateral cusp. However, the course of the coronary artery beyond the ostium was normal. The aorta presented a tremendous aneurysm in the ascending portion, measuring 22 cm. in circumference (Fig. 6). The intima appeared ruptured immediately above the cusps,

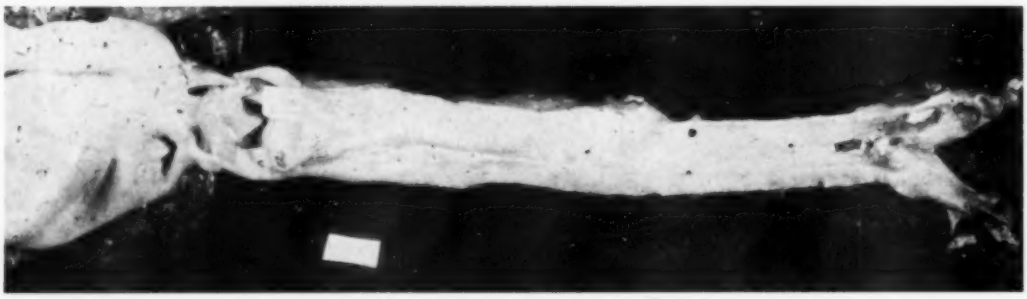

Fig. 7.—This specimen shows the dissection of the intima of the aorta throughout its entire length ending 2 cm. below the bifurcation in the iliac artery.

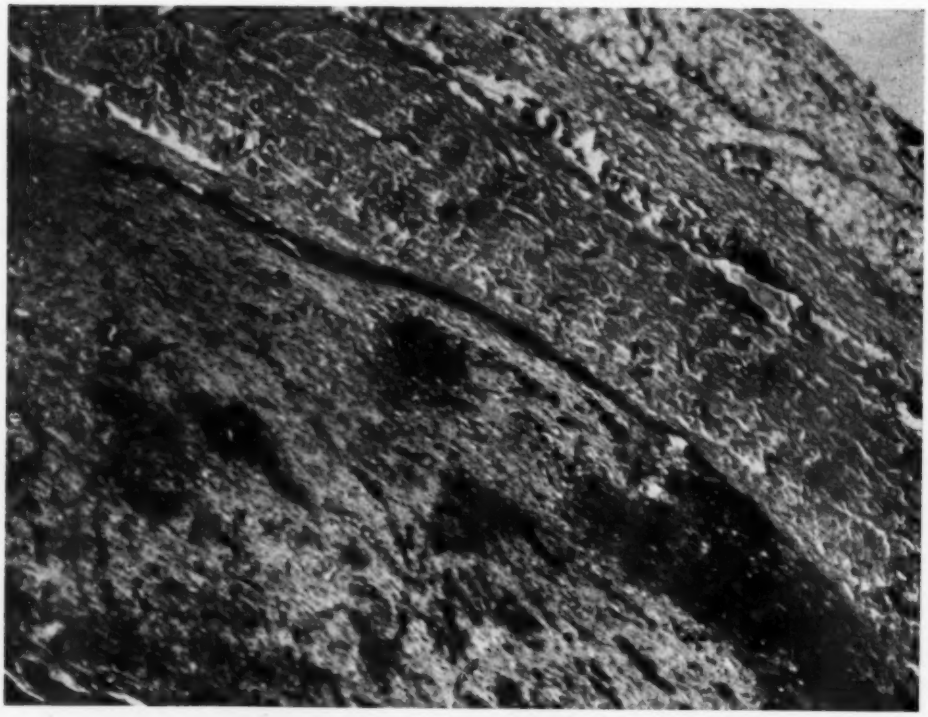

Fig. 8.—Section through the pericardium showing the strands of organized fibrin, new blood vessels, and multiple, active fibroblasts. There are numerous lymphocytes and macrophages.

and a denudated area measuring about 2 to 3 cm. in width and 15 cm. in length covered the media along the circumference. However, covering this area were granulation tissues. Immediately after the point at which the left subclavian artery arose there was another rupture of the intima, and at this point began a dissection of the intima of the aorta, throughout its entire length and ending 2 cm. below the bifurcation in the iliac arteries (Fig. 7). The pulmonary arteries were dilated. The lungs appeared emphysematous all over. The gall bladder was full of multiple, small, hard yellowish stones. The spleen was markedly enlarged. The uterus was hypoplastic and small, measuring 6 cm. in length, with half of this belonging to the cervix.

Microscopic: Sections of the heart revealed a thick layer covering the cardiac surface. This layer was formed by strands of organized fibrin, new blood vessels, and multiple, active fibroblasts infiltrating this layer. There were numerous lymphocytes and macrophages. The outer surface of this layer was formed by organizing fibrin. The pericardium revealed the same characteristics, with destruction of the inner layer. The myocardium, however, was not involved in this process (Fig. 8). The endocardium appeared thickened in the left auricle, with almost 1:1 ratio to the myocardium; however, there was no evidence of fibroelastosis. The mitral valve itself was not remarkable.

Sections of the aorta revealed medial necrosis with some cystic areas of basophilic changes. The lamellar pattern of the elastic fibers was disrupted. In the outer part of the media also there

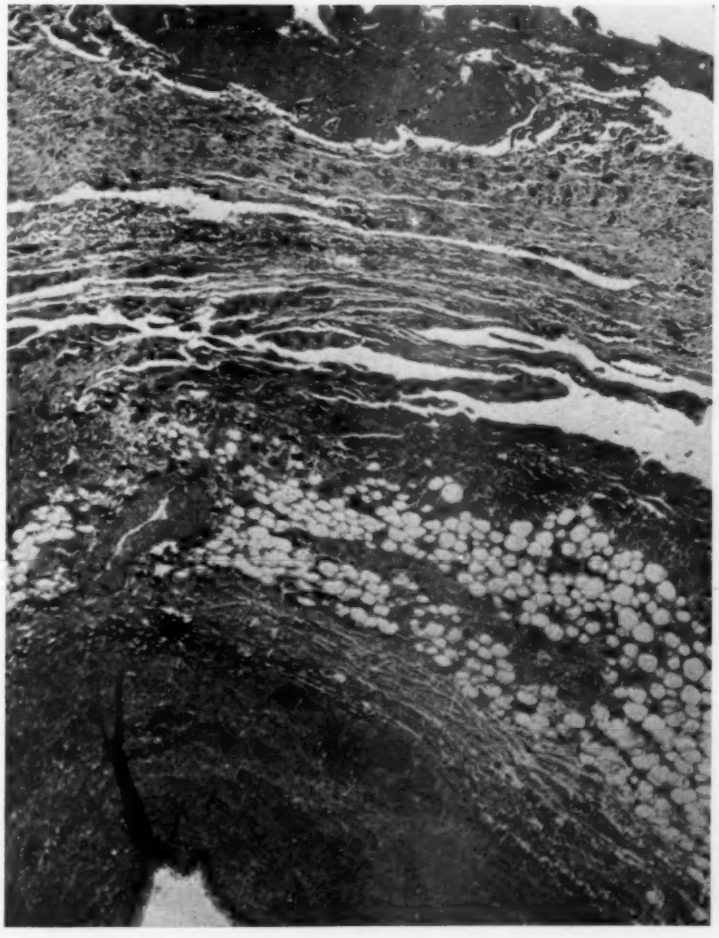

Fig. 9.—Section of the aorta showing medial necrosis with some cystic areas of basophilic changes.

were areas of hemorrhage and congested vasa vasorum. The intimal part of the aorta at places presented some plaques of atherosclerosis, while other areas showed almost a complete loss of this layer. The adventitia showed fibrin deposits infiltrated with new blood vessels and lymphocytes. The pulmonary artery revealed changes similar to those discovered in the media of the aorta (Figs. 9 and 10).

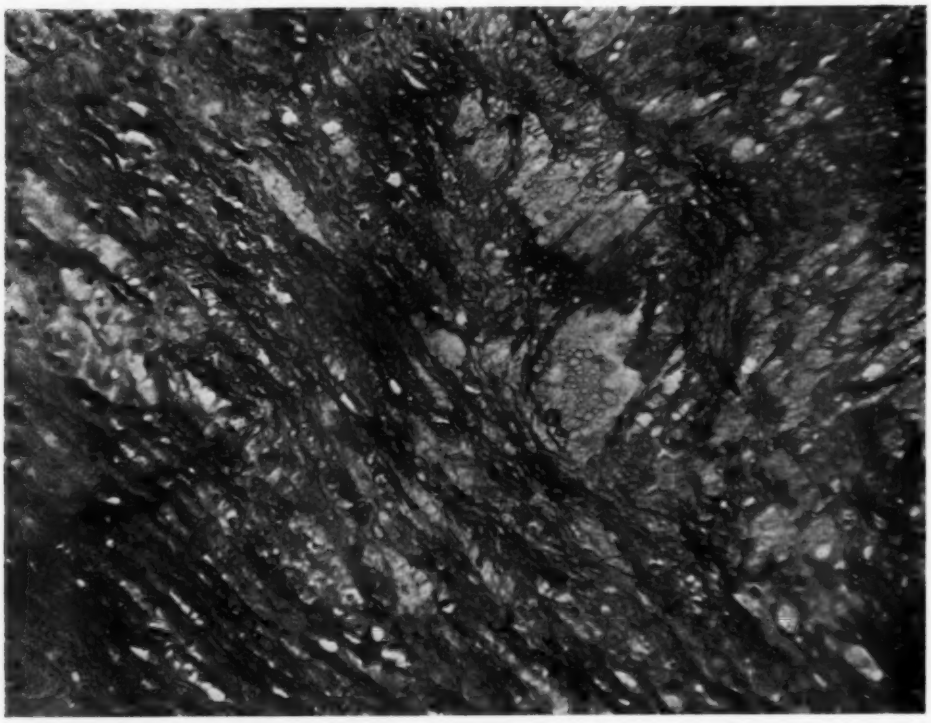

Fig. 10.—High magnification of a section of pulmonary artery showing medial necrosis, cystic areas of basophilic changes, and disrupted elastic fibers.

COMMENT

Taussig's case published in 1942, was the first reported case of Marfan's syndrome with aneurysmal dilatation of the ascending aorta.[3] In 1943, Glover[4] reported a case showing the dissecting aneurysm of the ascending aorta with acute fatal rupture into the pericardial sac. In 1947, Tobin[5] reported a case of dissecting aneurysm extending proximally to the aortic valve ring and peripherally to the iliac arteries. In 1947, Uyeyama[6] reported a large dissecting aneurysm of the aorta involving transverse, descending, and abdominal aorta. Up to 1947, 14 cases of Marfan's syndrome with autopsy had been reported.[5] Six of these had aortic involvement. Carroll's case reported in 1948,[7] was the fifth case of dissecting aneurysm in Marfan's syndrome. Marvel,[8] in 1951, reviewed all of the 28 autopsied cases of Marfan's syndrome. Since then 32 more autopsied cases have been added. Out of this total of 60 cases 33 had aneurysmal dilatation of the ascending aorta. A total of 18 had dissecting aneurysm of the aorta. Our case is another case of Marfan's syndrome with dissecting aneurysm of the

aorta. The unusual features to be noted in our case are: (1) presence of only one coronary ostium; (2) secundum type of atrial septal defect; (3) denudated granulating area in the ascending aorta; (4) unusually extensive dissecting aneurysm of the aorta extending 2 cm. below the bifurcation of the aorta; (5) dilatation of the pulmonary arteries; (6) shaggy necrotic pericarditis; (7) no sign of subacute bacterial endocarditis in the presence of fatal septicemia; and (8) markedly advanced emphysema. Our case did not show polyarachnodactyly or dislocation of the lens. However, the microscopic picture of the aortic wall was diagnostic of Marfan's syndrome. In addition, there was the typical medial necrosis of the wall of the pulmonary artery. This is a finding very rarely reported in the literature.[9,10] The clinical signs of aortic regurgitation in our case may be explained on the basis of a long dissecting aneurysm. The femoral systolic pressure was low because of the marked occlusion of the femoral arteries by the bulging aneurysm. The cyanosis is explained on the basis of atrial septal defect.

SUMMARY

A case of Marfan's syndrome is reported. Autopsy revealed many unusual features hitherto not reported in this condition.

REFERENCES

1. Griffin, F. J., and Koman, M. G.: Ann. Int. Med. **48**:174, 1958.
2. McKusick, A. V.: Circulation **11**:321, 1955.
3. Baer, R. W., Taussig, H. B., and Oppenheimer, E. H.: Bull. Johns Hopkins Hosp. **72**:309, 1942.
4. Etter, L. E., and Glover, L. P.: J.A.M.A. **123**:88, 1943.
5. Tobin, J. R., Bay, E. B., and Humphreys, E. M.: Arch. Int. Med. **80**:475, 1947.
6. Uyeyama, H., Kondo, B., and Kamins, M.: Am. Heart J. **34**:580, 1947.
7. Carroll, F. D.: Arch. Ophth. **40**:558, 1948.
8. Marvel, R. J., and Genovese, P. D.: Am. Heart J. **42**:814, 1951.
9. Tung, H. L., and Liebow, A. A.: Lab. Invest. **1**:382, 1952.
10. Anderson, M., and Pratt-Thomas, H. R.: Am. Heart J. **46**:911, 1953.

Valvular Pulmonic Stenosis: Auscultatory and Phonocardiographic Characteristics

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Until the advent of cardiac catheterization and more accurate diagnosis, pulmonic stenosis was considered a rare lesion. It is indeed a common congenital heart defect now, accounting for 10 to 15 per cent of the cases with congenital heart defects.[1,2] The significance of the pulmonic systolic murmur and the heart sounds associated with it has only recently been pointed out.[3,4] The majority of patients have no significant symptoms until late in the natural course of the disease. From an auscultatory and phonocardiographic view point, valvular pulmonic stenosis may be divided into three groups: mild stenosis, moderate stenosis, and severe stenosis.

Mild Stenosis.—A pulmonic systolic ejection murmur has usually been recorded following birth. The murmur may become louder with age. The intensity of the murmur may not be related to the severity of the stenosis, in that some of the harshest murmurs may occur with minimal stenosis. Varying with the intensity of the murmur, a thrill may be elicited over the pulmonic area. The first heart sound is almost always followed by an early systolic ejection sound (Fig. 1), giving the impression of accentuation or wide splitting of the first heart sound.[4,5] It varies markedly with respirations, becoming louder with deep expiration and diminishing or becoming inaudible with inspiration.[4] Shortly following the ejection sound is a harsh Grade 1 to 3 ejection-type systolic murmur, the bulk of which is confined to mid-systole (Fig. 2, top phono).

The pulmonic second sound is pathologically split, ranging from 0.03 to 0.06 second from the aortic component. This is related to delay in right ventricular ejection and subsequent delay in closure of the pulmonic valve, and there may be further widening with inspiration[4] (Fig. 1, bottom phono). The electrocardiogram and x-ray are usually normal except for poststenotic dilatation of the pulmonary artery. The pulmonary blood flow usually appears normal. The electrocardiogram is usually normal but may show varying degrees of right ventricular hypertrophy.

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Moderate Stenosis.—The ejection sound is usually present, the murmur is mid- to late systolic, and the pulmonic component is further delayed 0.06 to 0.10 second after the aortic. Diminished pulmonary blood flow is usually present radiographically. The electrocardiogram shows right ventricular hypertrophy.

Severe Stenosis.—Severe pulmonic stenosis differs from the former groups in that the systolic murmur is further delayed, overriding the aortic component of the second sound (Fig. 3). This can best be appreciated by noting the prolongation of the murmur past the end of the carotid pulsation. With severe degrees of stenosis and heart failure the murmur may be absent in rare instances. Right ventricular hypertrophy and pulmonary ischemia are usually obvious on x-ray examination. In the majority of cases the pulmonic component of the second sound is audible and recordable, but markedly delayed (0.10 to 0.14 second) after the aortic component (Fig. 2). The intensity of the pulmonic component is related to the degree of delay of ejection of the right ventricle and subsequent closure of the valve.[4]

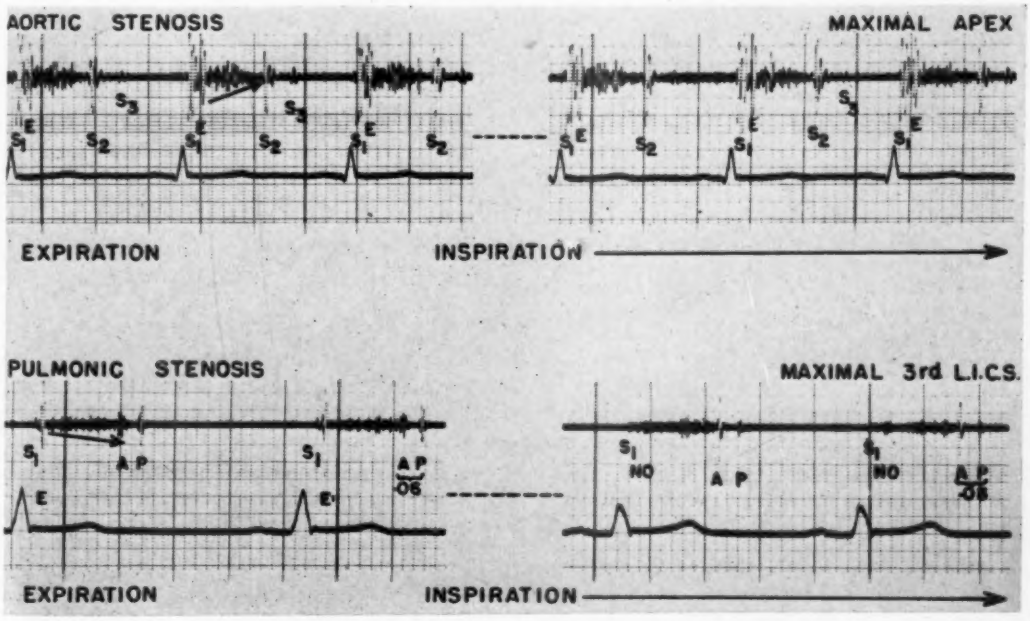

Fig. 1.—Aortic and pulmonic ejection sounds. S_1-S_2-S_3 = First, second, and third heart sounds. *A* = Aortic component of second sound; *P* = pulmonic component of second sound. The ejection sound (*E*) with aortic stenosis persists throughout the respiratory cycle and may be maximal at the apex. The ejection sound (*E*) with pulmonic stenosis varies markedly, with respirations diminishing or becoming absent with inspiration and reappearing with expiration. The pulmonic second sound with pulmonic stenosis is pathologically split and widens further with inspiration. (Stethograms sen. 4. Paper speed 75 mm./sec.)

With relief of pulmonic obstruction by valvulotomy, the murmur changes and may now occupy early to mid-systole, corresponding to the shift in maximum ejection of the right ventricle. The pulmonic component of the second sound increases in intensity and moves in closer to the aortic component of the second sound[4] (Fig. 4).

In our experience the pulmonic ejection sound may or may not be present with severer degrees of stenosis (Fig. 3), but it is frequently absent because the marked prolongation of ejection and diminution of flow into the pulmonary artery is unable to rapidly change pulmonary arterial tension which produces the sound.

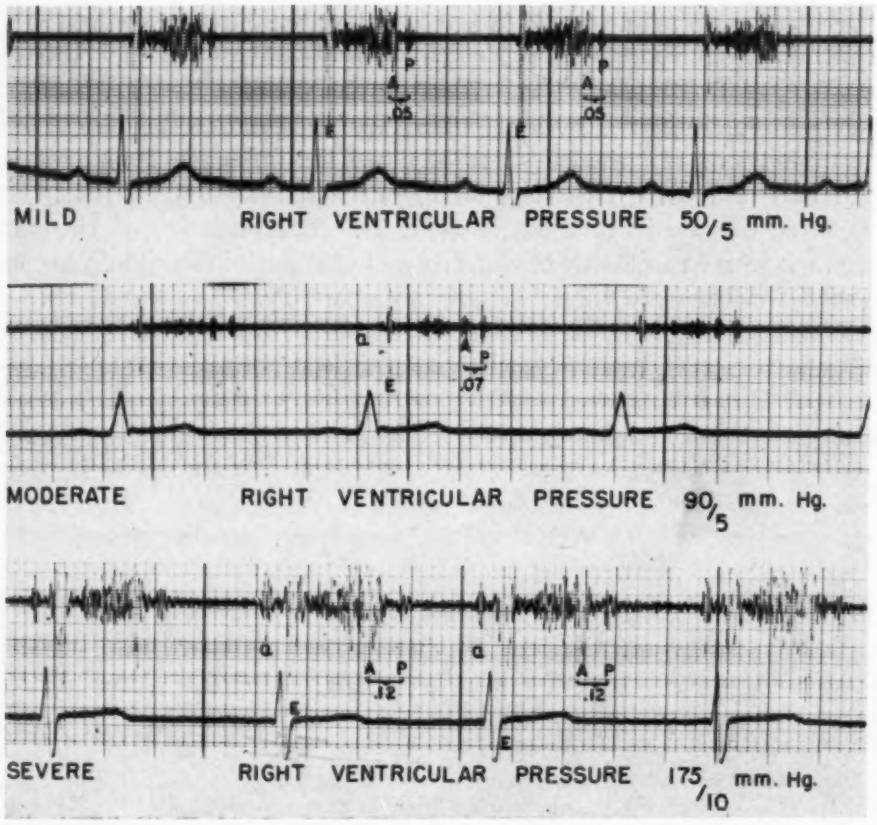

Fig. 2.—The bulk of the murmur with mild pulmonic stenosis is confined to mid-systole. There is a close linear correlation with the delay in pulmonic valve closure (*P*) and right ventricular systolic pressure as illustrated by the A-P interval. *A* = Aortic component of second sound; *E* = ejection sound; *a* = fourth heart sound. (Stethograms paper speed 75 mm./sec.)

EJECTION SOUND IN PULMONIC STENOSIS

The ejection sound with pulmonic stenosis occurs on an average of 0.08 second after the onset of the rise of pressure in the pulmonary artery (Fig. 5). It is not related to the opening of the semilunar valves or closure of the atrioventricular valves.[5] It is present over the naked pulmonary artery at operation. Satisfactory pulmonary arterial tracings showing the relationship of pulmonary arterial pressure curves to the ejection sound have been difficult to obtain. In Fig. 5 is a satisfactory tracing, which was duplicated in another patient (Fig. 6). There is tremendous poststenotic turbulence of flow in the pulmonary artery, transmitting kinetic forces into lateral pressures and accounting for poststenotic dilatation of this vessel.[6] Because of the nature of turbulent flow there

is marked fluctuation of pulmonary arterial pressure, as previously noted and as shown by the staircase nature of the curve. With resting expiration the ejection sound is constantly present and coincides with the initial ejection phase (*I*) in the pulmonary arterial trace (allowing for a delay of 0.02 second). It would

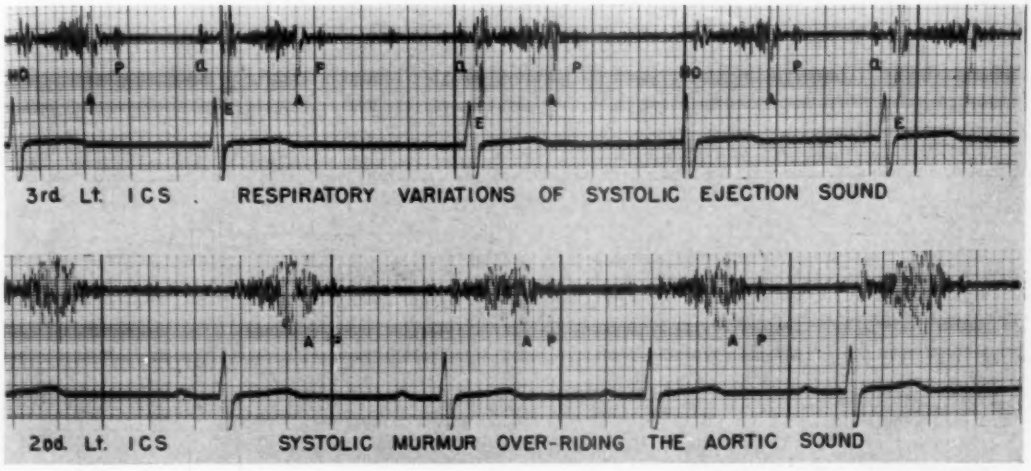

Fig. 3.—The bulk of the systolic murmur is delayed past mid-systole in severe pulmonic stenosis and may override the aortic component (*A*) of the second sound. Note the striking fluctuation of the fourth heart sound (*a*) and ejection sound (*E*) with respiration. *NO* = Absent. *P* = Pulmonic component of second sound. (Stethograms sen. 5. Paper speed 75 mm./ sec.)

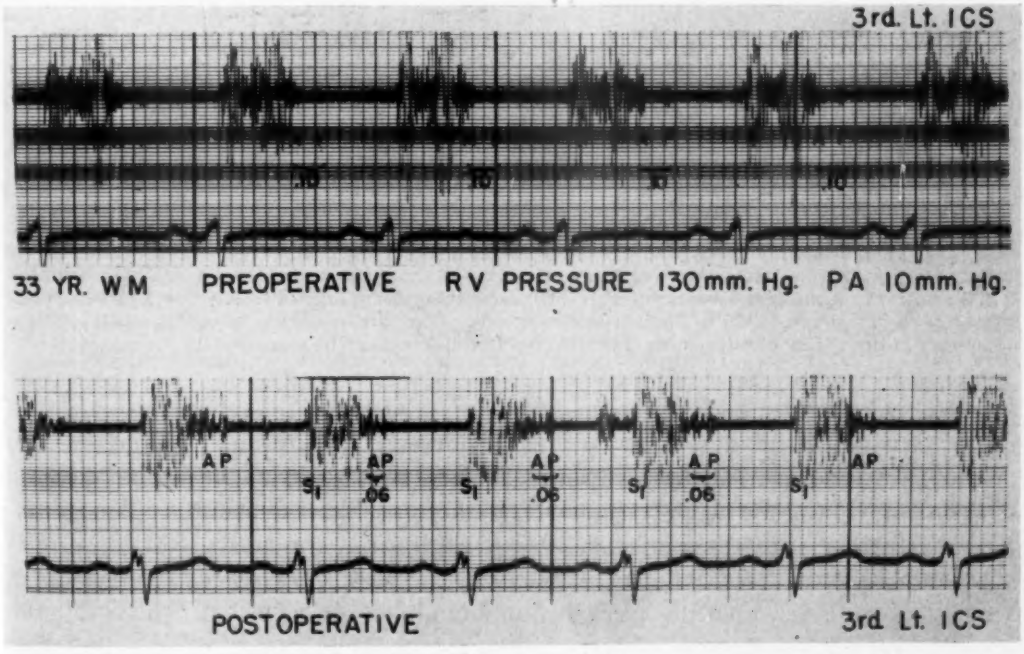

Fig. 4.—With relief of the obstruction by pulmonic valvulotomy, the murmur now occupies early systole, and the pulmonic component (*P*) of the second sound increases in intensity and moves in closer to the aortic component (*A*) of the second sound. S_1 = First heart sound. (Stethograms sen. 5. Paper speed 75 mm./sec.)

seem that with inspiration, increases in negative intrathoracic pressure and mechanical stretch from distention of the lungs and descent of the diaphragm make the thin-walled, poststenotic pulmonary artery area taut, and the initial ejection of blood (*I*) into the pulmonary artery is unable to suddenly change the distensibility of this vessel and produce the high-pitched clicking sound. The

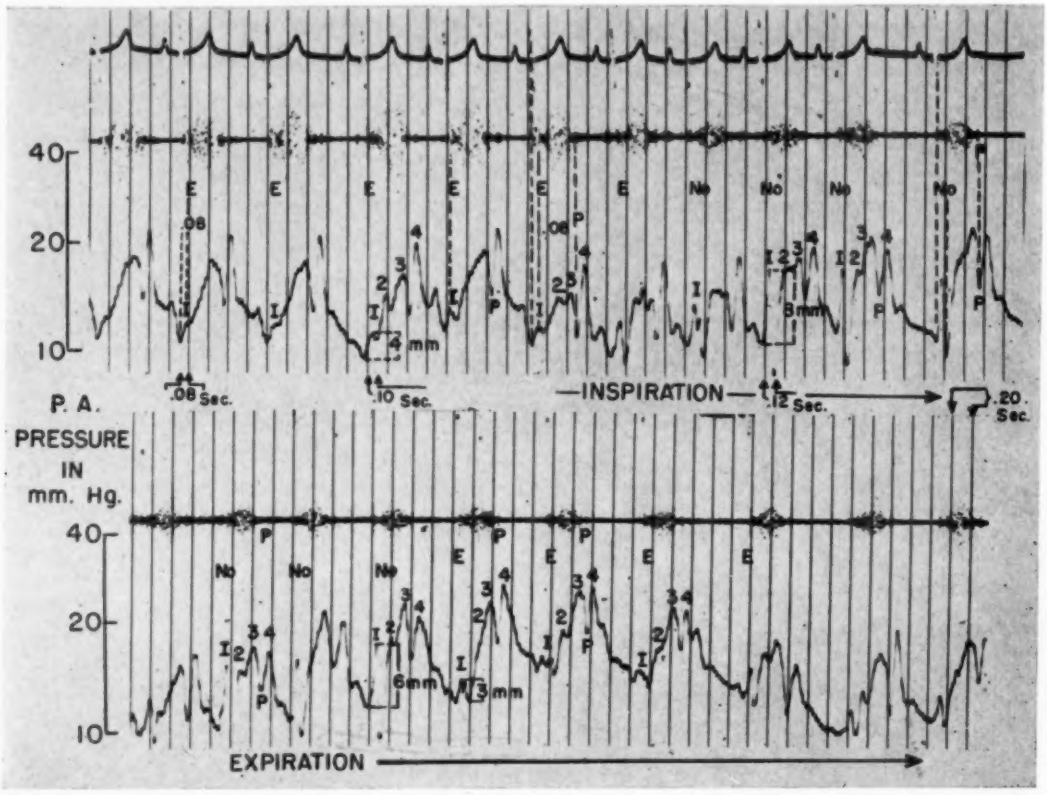

Fig. 5.—With inspiration note the increase (3 to 8 mm. Hg) in magnitude of the initial rise in pressure (*I*) in the pulmonary artery and disappearance of the ejection sound (*E*). With expiration the initial pressure increase diminishes from 7 to 4 mm. Hg, and the ejection sound reappears. The numbers *2, 3, 4* arbitrarily identify the remaining pulmonary arterial pressure fluctuations. *P* = Pulmonic component of second sound. *NO* = Absent ejection sound. The same sequence of events was duplicated in another patient (Fig. 6). (Phonos: logarithmic filter; paper speed 25 mm./sec.)

increase in magnitude of the initial forces (*I*) and recoil reflect the alteration in initial tension of the vessel, as well as an increase in rate and volume ejection of the right ventricle with inspiration. If alteration in right ventricular ejection with inspiration alone were responsible, it should make the sound louder or displace it further into the murmur. With expiration, the poststenotic area becomes slack, and the initial ejection phase of the right ventricle produces sudden tensing of the area, creating the ejection sound. This situation can be demonstrated best with a sheet of paper. When the paper is tensed, sudden increases in tension produce no significant sound, but when the paper is slack, a sudden increase in tension produces a striking sound. It is not a contact sound because it is present over the naked pulmonary artery at operation. An aortic ejection

sound varies little with the respiratory cycle, probably because of the thickness and stability of the aorta, which is uninfluenced by changes in respiration (Fig. 1, top phono).

THE SECOND SOUND

The pulmonic second sound is pathologically split and this splitting is audible and recordable in the majority of cases of pulmonic stenosis.[4] The first component is aortic and the second is pulmonic.[7] With pulmonic stenosis there is a greater resistance to right ventricular outflow, with delay of ejection and subsequent closure of the pulmonic valve. We have been able to corroborate Leatham's observations that there is an excellent linear correlation between the degree of stenosis as reflected by the aorticopulmonic interval and right ventricular systolic pressure[4] (Fig. 2).

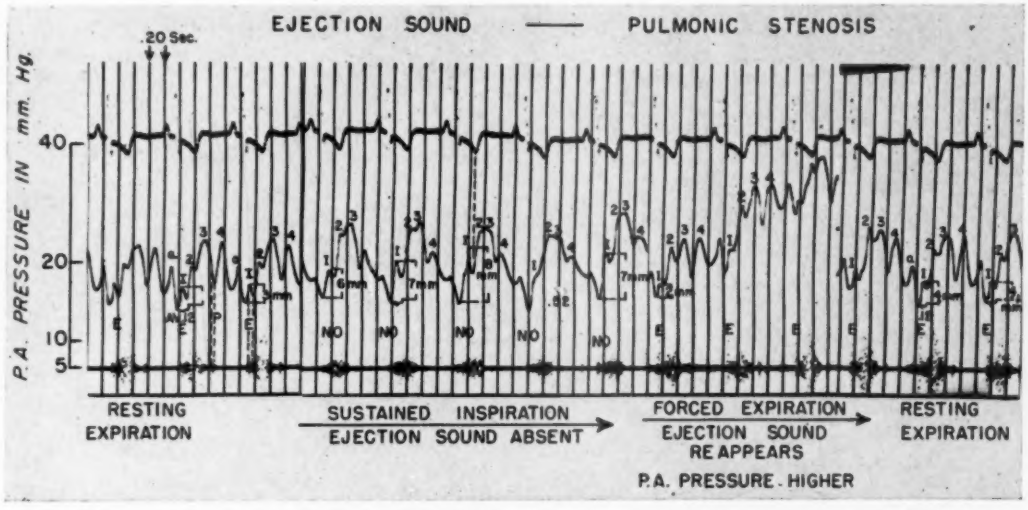

Fig. 6.—Duplication of the tracing in Fig. 5, from another patient showing the same respiratory relationships between the initial pressure rises in the pulmonary artery (*I*) and the presence or absence of the ejection sound (*E*).

Method.—A Sanborn twin-beamed phonocardiograph was used to record heart sounds, using the logarithmic filter.

The aortic component was identified by matching comparable cycles of apex phonocardiograms with those taken in the third left intercostal space at resting expiration. The aortic component is transmitted well to the apex, while the pulmonic component is rarely recorded there.[7] The majority of tracings were made in close proximity to catheterization, and there is little variation in the aorticopulmonic interval from beat to beat at quiet resting expiration. The interval was measured from the beginning of the aortic component to the beginning of the pulmonic component. The reliability of this method was substantiated by phonocardiograms taken during simultaneous cardiac catheterizations (Figs. 6 and 7).

In Fig. 7 are 10 consecutive cases of pulmonic stenosis in which the aorticopulmonic interval is correlated with right ventricular systolic pressure. The

method of linear correlation is excellent and far superior to that using the height of the R wave in Lead V_1 in the same 10 patients (Fig. 8). The former method is a valuable and inexpensive aid in the estimation of right ventricular systolic pressure in regard to follow-up and ultimate selection of patients for surgery. The pitfalls in recording this interval are: (1) a small day-to-day variation of 0.02 second, related to alterations in right ventricular contractility; (2) recording at resting expiration when the sounds are closest and with right ventricular inflow as stable as possible; (3) a breakdown of linear correlation with very low and very high degrees of stenosis; (4) inability to record the pulmonic second sound (but this in itself is a valuable sign of severe stenosis[4]).

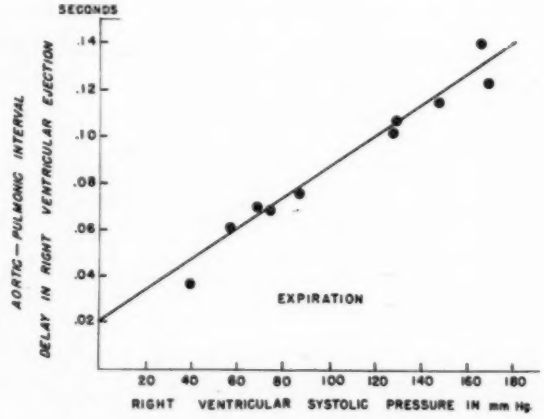

Fig. 7.—The correlation of the aortic and pulmonic intervals by phonocardiography with right ventricular systolic pressure at catheterization has a close linear relationship and is superior to the method using the height of the R wave in Lead V_1 in the same 10 patients (Fig. 8).

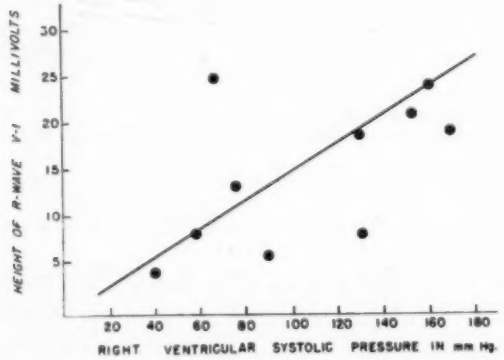

Fig. 8.—The height of the R wave in Lead V_1 in the same 10 patients as in Fig. 7 is correlated with right ventricular systolic pressure.

DISCUSSION

There are several murmurs occurring in the pulmonic area which are commonly confused with mild valvular pulmonic stenosis. Electrocardiography and fluoroscopy of the chest may be of little help, because the findings by these

means are usually within normal limits. Electrocardiography may even be misleading in children, showing right ventricular preponderance with the murmur of aortic stenosis maximal in the pulmonic area or mid-sternum, thereby indicating a diagnosis of pulmonic stenosis. The auscultatory and graphic characteristics of the murmurs and accessory sounds provide the real clues in differentiation. Atrial septal defect differs in several ways. The murmur is an early systolic flow murmur of much less intensity. There is wide, fixed splitting of the second sound.[8] There is a prominent left parasternal lift and diastolic filling sound, a reflection of a large left-to-right shunt. A pulmonic ejection sound occurs less frequently than in pulmonic stenosis.

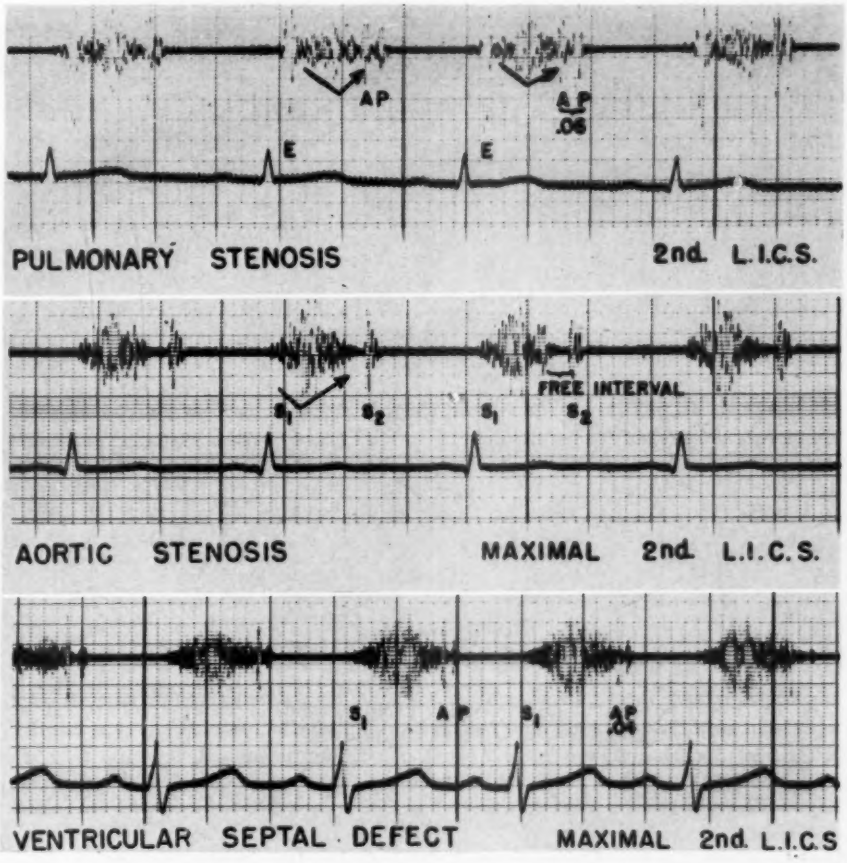

Fig. 9.—The graphic features of stenotic pulmonary systolic murmurs occurring in the second left intercostal space are contrasted. The ejection sound (*E*) and second sound (S_2) (*A*, *P*) are the best means of differentiation, since aortic stenosis and ventricular septal defect occasionally are maximal in the second left intercostal space, simulating pulmonic stenosis (see text). (Paper speed 75 mm./sec.)

Aortic stenosis and ventricular septal defect occasionally are maximal in the second left intercostal space (Fig. 9). The murmurs all may be diamond-shaped, but mild aortic stenosis occupies early systole, ending well before the aortic second sound, which is narrowly split or single, related to merger of the

aortic and pulmonic components of the second sound. The ejection sound with aortic stenosis is usually maximal at the apex and varies little with respirations. Ventricular septal defect is pansystolic, ending with a second sound which is normally split and of normal intensity as long as pulmonary arterial pressure is normal.[9] A loud ventricular filling sound (S_3) is usually present, and its magnitude parallels the degree of shunt.[9]

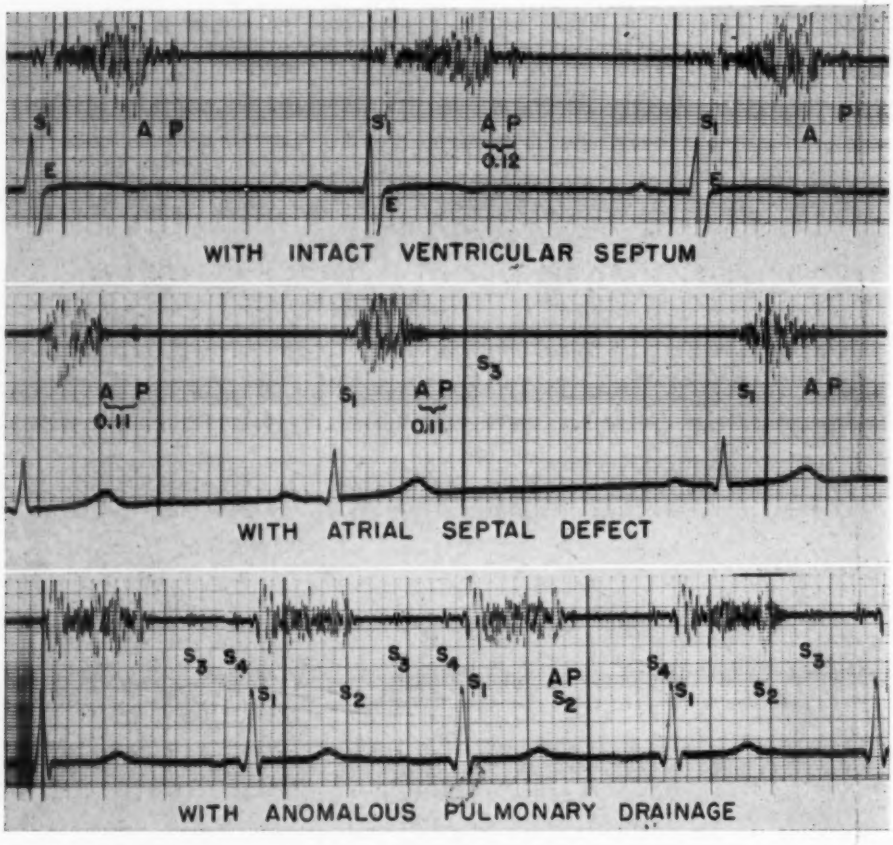

Fig. 10.—A third heart sound (S_3) reflecting rapid ventricular filling or dilatation is unusual in compensated moderate to severe pulmonic stenosis, and when present, it is a valuable clue to the presence of an associated defect or shunt, namely, atrial septal defect and/or anomalous pulmonary venous drainage. S_1 = First heart sound; S_2 = second heart sound; S_4 = fourth heart sound. A-P = Aortic and pulmonic components of second sound (S_2).

When a ventricular filling sound (S_3) (Fig. 10) is present with moderate to severe compensated pulmonic stenosis, either atrial septal defect or anomalous pulmonary veins, or both, are usually present. This is related to rapid ventricular filling produced by the added shunt. This observation has been a valuable clue to the association of pulmonic stenosis with other lesions. In the cyanotic child the wide splitting of the second sound and associated ventricular filling sound are helpful in differentiating pulmonic stenosis with atrial septal defect from tetralogy of Fallot, where the second sound is usually single and a third sound is rarely heard.

SUMMARY

1. Mild pulmonic stenosis has an early systolic ejection sound and a characteristic mid-systolic ejection murmur followed by pathologic splitting of the second sound. The aorticopulmonic interval by phonocardiography is 0.03 to 0.06 second, and right ventricular systolic pressure is usually less than 60 mm. Hg.

2. Moderate pulmonic stenosis has an aorticopulmonic interval of 0.06 to 0.10 second, and right ventricular pressure ranges from 60 to 100 mm. Hg.

3. Severe pulmonic stenosis has a late systolic ejection murmur which may override the aortic second sound. The pulmonic second sound is markedly delayed in closure, and an ejection sound may or may not be present. The aorticopulmonic interval is usually 0.10 to 0.14 second, and right ventricular systolic pressure is more than 100 mm. Hg. There is the usual overlap of the groups.

4. We have been able to further corroborate Leatham's observations that there is a close linear relationship between the degree of stenosis as reflected by right ventricular systolic pressure and the delay in closure of the pulmonic valve. This is a valuable aid in assessing the status of pulmonic stenosis, and is more reliable than using the height of the R wave in Lead V_1.

5. We believe that the pulmonic ejection sound which disappears with inspiration and reappears with expiration is related to mechanical alterations in the initial tension of the poststenotic pulmonary artery, owing to the respiratory cycle. The aortic ejection sound varies little with the respiratory cycle.

6. When a ventricular filling sound (S_3) is present with moderate to severe pulmonic stenosis, an atrial septal defect and/or anomalous pulmonary venous drainage is usually associated with it.

7. Aortic stenosis and ventricular septal defect both may present as stenotic-type murmurs, maximal in the second left intercostal space, simulating pulmonic stenosis. The graphic character of the systolic murmur, second sound, and ejection sounds are the best means of differentiation, because location, electrocardiography, and x-ray may be of little value in the mild defects.

REFERENCES

1. Wood, P.: Brit. M. J. **2**:639, 1950.
2. Adams, F. H.: J. Pediat. **38**:431-441, 1951.
3. Abrahams, D. G., and Wood, P.: Brit. Heart J. **13**:519, 1951.
4. Leatham, A., and Weitzman, D.: Brit. Heart J. **19**:303, 1957.
5. Leatham, A., and Vogelpoel, L.: Brit. Heart J. **16**:21, 1954.
6. Kjellberg, S., Mannheimer, E., Rudhe, U., and Jonsson, B.: Diagnosis of Congenital Heart Disease, Chicago, 1955, The Yearbook Publishers, Inc., p. 141.
7. Leatham, A.: Lancet **2**:607, 1954.
8. Leatham, A., and Gray, I.: Brit. Heart J. **18**:193, 1956.
9. Mannheimer, D., Tkkos, D., and Jonsson, B.: Brit. Heart J. **19**:333, 1957.

Congenital Stenosis of Pulmonary Veins at Their Atrial Junctions

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This case presentation concerns an infant who died of cor pulmonale due to congenital obstruction of three of the five pulmonary veins at their atrial terminations. This exceedingly rare congenital anomaly permits observation of the changes produced in pulmonary tissue by severe stenosis of the pulmonary veins. Also, anatomic study indicates that surgical correction of this type of stenosis is probably feasible. For these reasons, this case is published in detail.

CASE REPORT

Clinical Course.—This 8½-month-old white boy was last admitted to the Children's Hospital of Pittsburgh on May 4, 1957, because of "failure to do well."

Both parents were suffering from hay fever, and one sibling from asthma. The remaining three siblings were enjoying good health.

Pregnancy and delivery had been uncomplicated. The birth weight was 3,320 grams. The neonatal period was not remarkable. His mother, considered to be a reliable informant, stated that his progress had been normal until he was about 3½ months of age, when he began to eat poorly and developed "one cold after another." These "colds," which consisted of episodes of fever, cough, and noisy breathing, failed to respond to a variety of antibiotics. It was during one of these episodes that his pediatrician suspected enlargement of the heart and pneumonia. For these reasons the patient was admitted for the first time on March 21, 1957. On admission his rectal temperature was 102° F., and he was in respiratory distress as evidenced by retraction of intercostal spaces and rapid respiratory rate. Coarse râles were heard throughout the chest. There was no change to percussion. There were no thrills nor murmurs, and the femoral pulses were easily palpated. The liver was 1.0 cm. below the costal margin, and there were no other palpable abdominal masses. During this admission, chest films revealed widely disseminated, stringy shadows of increased density lying almost exclusively posteriorly. (These shadows had not completely disappeared at the time of discharge.) Enlargement of the pulmonary conus was also noticed on the films, and there was right axis deviation on the electrocardiogram. Urinalysis was normal. Hemoglobin was 10.0 Gm./100.0 ml. The hematocrit was 32 per cent. The white blood cell count was 14,150/mm.^{3}, with 64 per cent polymorphonuclear leukocytes, 5 per cent metamyelocytes, 28 per cent lymphocytes, 1 per cent monocytes, and 2 per cent eosinophils. Blood urea nitrogen and serum electrolytes were within normal limits. Total protein was 7.3 Gm./100 ml. A sweat test helped to rule out mucoviscidosis (chloride 17.4 mEq./L. and sodium 14.0 mEq./L). Trypsin was present in the stools. Intradermal tuberculin test (1:100, OT) was negative. Blood culture proved sterile. Culture of the throat yielded *Escherichia coli, N. catarrhalis,*

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and β hemolytic streptococci. Therapy consisted of penicillin, streptomycin, and oxygen. The progress was slow, but the physical signs of pulmonary disease cleared, and the child was discharged on April 14, 1957.

After discharge there was a short period of improvement, but symptoms returned, and on the day before his second and last admission on May 4, 1957, cough accompanied by vomiting developed.

Physical findings on his last admission revealed increased resonance of the chest. Râles were not heard but breathing was noted to be "noisy." P_2 was greater than A_2. No murmurs nor thrills were present. The point of maximal impulse was within the mid-clavicular line. The liver was 1.0 cm. below the costal margin, and there were no other abdominal masses. His hemoglobin was 9.8 Gm./100 ml. The hematocrit was 35 per cent. The white blood cell count was 22,200/mm.^{3}, with 68 per cent polymorphonuclear leukocytes, 3 per cent metamyelocytes, 28 per cent lymphocytes and 1 per cent eosinophils. A total eosinophil count was 220/mm.^{3} Urinalysis revealed a specific gravity of 1.030, pH 5.5, albumin 2+, and sugar negative. *Micrococcus pyogenes* var. *albus* and β hemolytic streptococci were grown from the nose. Cultures of the blood and spinal fluid yielded no growth. The spinal fluid was clear and contained no cells. A roentgenogram of the chest revealed increased densities in the hilar portions of the lungs. The heart was moderately enlarged, and the apex rounded. The right atrium was enlarged and the pulmonary conus was prominent (Fig. 1). On the second hospital day the child was noted to be dyspneic and pallid. His pulse rate was 150 per minute. Fine râles had appeared in the right posterior chest. Although he was critically ill, death was not anticipated when it occurred on May 6, 1957.

Autopsy Findings.—The anatomic cause of death was extreme pulmonary hyperemia with edema and multiple hemorrhages of the lungs. These changes were associated with cor pulmonale secondary to congenital pulmonary vein obstruction. Changes of interest were limited to the thoracic organs.

Gross examination: The heart and lungs were not weighed because they were kept together with the mediastinal tissues as a single specimen.

Cardiomegaly due to right-sided dilatation and hypertrophy was quite marked (Fig. 2). The greatest transverse diameter of the heart was 7.0 cm., while the chest at the same level measured 11.0 cm. The right ventricular myocardium was reddish-brown and uniformly firm. It was 6.0 mm. thick in both the lateral wall and the conus. This measurement did not include the markedly hypertrophied trabeculae carneae. The apex of the heart was markedly rounded and was composed of right ventricular myocardium. There was slight patchy clouding of the ventricular endocardium, but there was no true opacity. The pulmonary artery had an outside diameter of 21.0 mm., as compared to 11.0 mm. for the aorta. The ductus arteriosus was obliterated. The right atrium was dilated and it had a thin wall. The foramen ovale was probe-patent, and the orifice of the coronary sinus was not unusual. There was no alteration of tricuspid or pulmonic leaflets. The left ventricle was of average size and was unaltered.

The primary alteration was in the pulmonary veins at their junctions with the left atrium (Fig. 3). There were five pulmonary veins, one from each lobe. The veins draining the left upper and right middle lobes were widely patent and were unaltered. The orifices of the three veins draining the right upper and both lower lobes were stenotic on gross examination. None of these orifices would admit a fine probe. In none of these veins was the stenotic portion more than 5.0 mm. long. The obstruction in each instance began at the atrial endocardial surface and extended along the course of the veins. The narrowing consisted of intrinsic thickening of the walls without change in the external diameter of the veins. Only minimal dilatation of these veins was noticed as they were opened through the unobstructed portions of their extrapulmonary courses. There was no significant hypertrophy of the vessel walls on the pulmonary side of the obstruction. No hint of the obstruction was detectable from external inspection, but the obstructed veins from the lower lobes were placed more superiorly than usual, inserting at a level with or slightly superior to the veins from the upper lobes. The pale, unstained intimal surfaces were smooth. There was no evidence of thrombosis, either recent or old.

Mediastinal dissection of the fixed specimen revealed five small peribronchial veins, all less than 1.0 mm. in diameter, to extend from the hilum of the right lung to the mediastinum, where they joined the mediastinal veins, and formed plexuses about the mediastinal lymph nodes (Fig. 4).

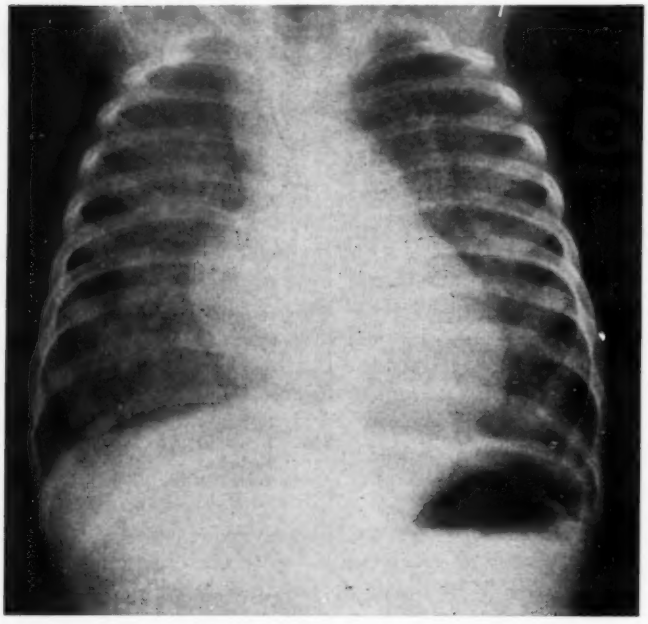

Fig. 1.—This posteroanterior film of the chest (5-4-57) shows enlarged pulmonary conus and right atrium The vascular markings are increased in the lung fields.

Fig. 2.—Right ventricular hypertrophy is accompanied by enlargement of the pulmonary artery and lungs that remain voluminous after removal.

Fig. 3.

Fig. 4.

Fig. 3.—In this posterior view of the opened left atrium, the lungs have been turned so that their apices point toward the apex of the heart. The vein from the left upper lobe is patent and lies inferior to the obstructed left lower lobe vein.

Fig. 4.—Moderate enlargement of bronchial and mediastinal veins is demonstrated in this photograph.

Drainage of the mediastinal veins was into the superior vena cava. Four similar peribronchial veins were found extending from the left hilum into the mediastinum. Enlargement of the mediastinal vein orifices in the superior vena cava was equivocal.

The lungs collapsed only slightly when the thorax was exposed. The pleural surfaces were smooth and shining, and varied from dark brown to purple in the right lower lobe. They were pale brown elsewhere. These lungs were subcrepitant, and when compressed, tended to spring back to their original shape. The right lower lobe was different in consistency from the rest of the lung. It was uniformly firm and contained large, irregular, blotchy regions of hemorrhage. Two small, firm, irregular nodular regions could be palpated in the left lower lobe. There was no obstruction of the pulmonary arteries or the bronchi.

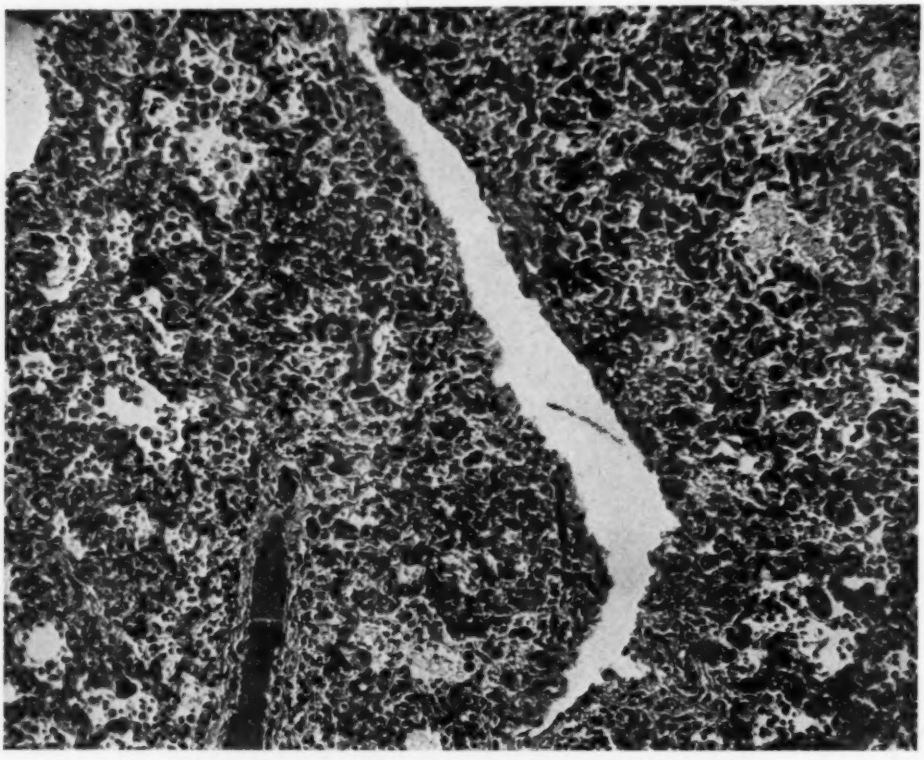

Fig. 5.—This field is typical of the capillary hyperemia and exudation of macrophages found in patchy regions throughout the obstructed lobes and occasionally in the unobstructed lobes. Hematoxylin and eosin, magnification × 140.

Microscopic description: Sections made from obstructed and unobstructed lobes were compared. Both contained small focal regions of air-containing alveoli. However, most of the parenchyma, especially in the lobes drained by the stenotic veins, showed severe capillary distention and hyperemia (Fig. 5). This hyperemia was frequently accompanied by protein-rich edema fluid, which lay in the alveolar spaces and extended in some regions to alveolar ducts and bronchioles. In the latter positions this fluid stained densely and had the fibrillar quality of fibrin. Hemorrhage was present only in a few focal regions. Many intra-alveolar macrophages were disseminated throughout. These macrophages tended to have dense eosinophilic cytoplasm, and small, dark, centrally placed nuclei. Some were multinucleated, containing as many as four nuclei. Erythrophagocytosis was occasionally observed, but hemosiderin was present in only a few of these cells. Patchy regions of atelectasis with fibrous thickening of alveolar walls were scattered throughout the obstructed lobes. Acute exudate was conspicuously absent, except in the right lower lobe, where it was patchy and minimal.

Proliferative thickening of the muscular coats of pulmonary arterioles was the most striking vascular change. There was no essential difference in this change in the obstructed and the unobstructed lobes (Figs. 6 and 7). The smaller the arteriole, the more severe was this change.

Fig. 6.

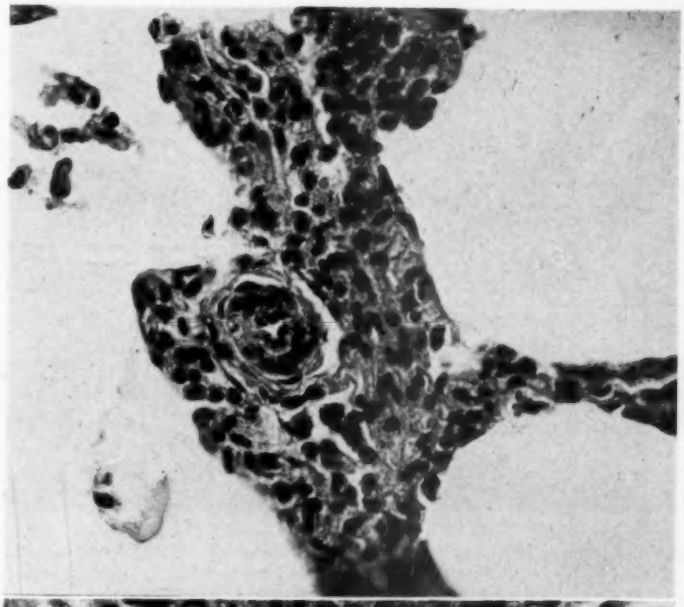

Fig. 7.

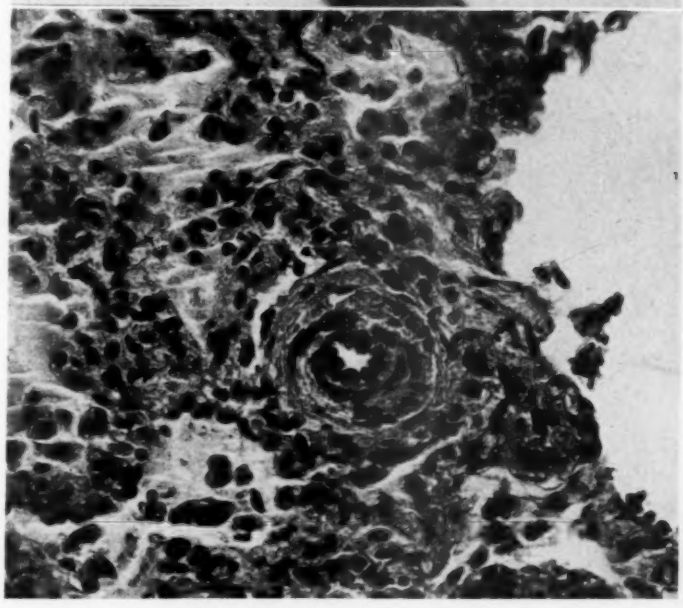

Fig. 6.—Stenosis of an arteriole with thickening of the muscular coat is demonstrated. Note, also, the interstitial exudate (chiefly macrophages). This photomicrograph was taken from the obstructed left lower lobe. Hematoxylin and eosin, magnification × 300.

Fig. 7.—Arteriolar change similar to that shown in Fig. 6 is seen in the unobstructed left upper lobe. Hematoxylin and eosin, magnification × 300.

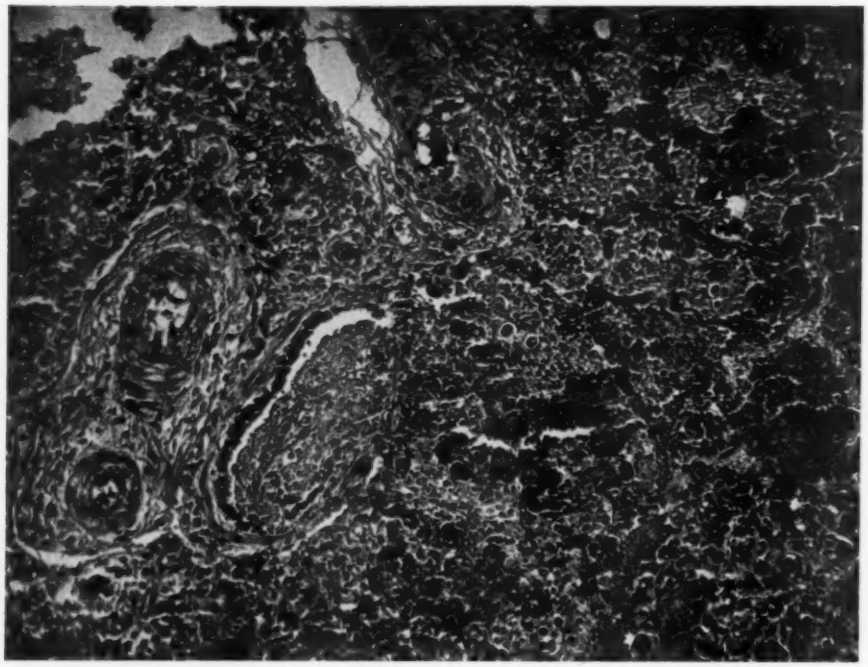

Fig. 8.—Alveolar hemorrhage, macrophages, and fibrin-like material are seen in this photomicrograph from the right lower lobe. A bronchiole is occluded by the fibrin-like material; arteriolar changes may also be seen. Hematoxylin and eosin, magnification × 140.

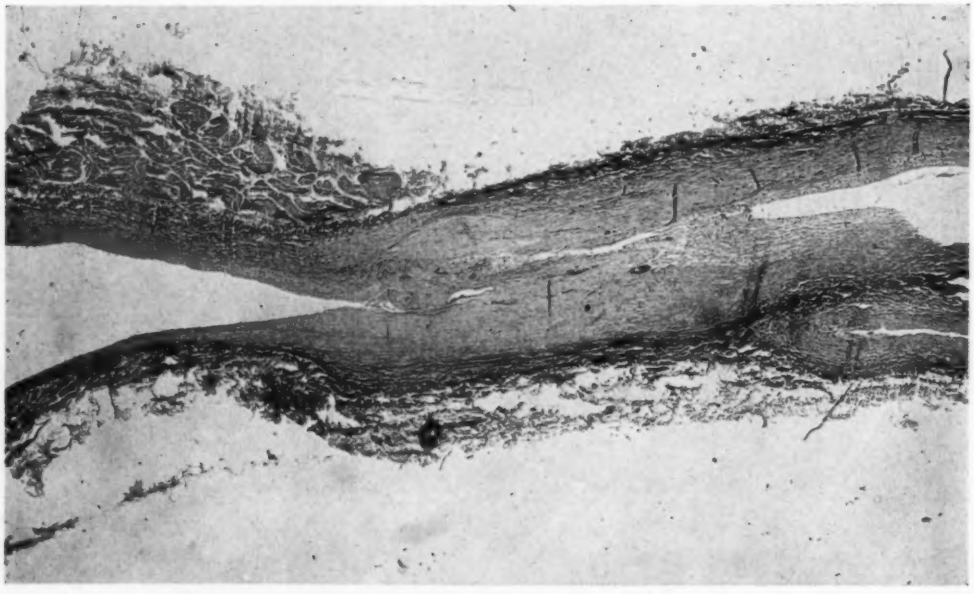

Fig. 9.—In this longitudinal section through the obstructed vein from the left lower lobe, the atrial wall lies to the left. The extremely stenotic lumen is discontinuous in this single section because of its tortuosity. Note the abrupt ending of myocardial fibers at the atrial junction to the left of the photograph. Hematoxylin and eosin, magnification × 9.

Large arteries were altered only by dilatation, minimal fraying of elastica, and rare patches of mild intimal fibrosis. The veins were dilated, more so in the subpleural than in the hilar location. There was some fibrous and edematous thickening of the pleura. Pleural veins were not included in the sections, but were not conspicuous grossly.

Hyperemia in the solid right lower lobe was similar to that in the other lobes, but more severe. Small patchy foci of necrotic alveolar walls with accompanying hemorrhage were present in this lobe and absent elsewhere. The protein-rich edema fluid was more widely disseminated in this lobe than elsewhere, and it extended well into the bronchi (Fig. 8). It was accompanied by occasional small collections of granulocytes.

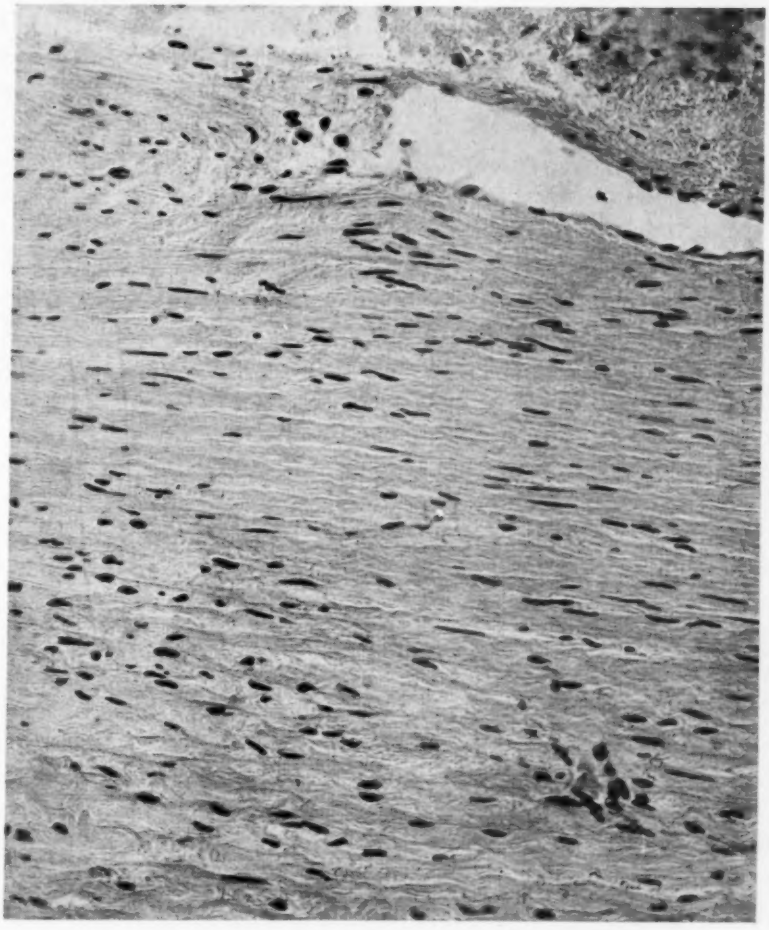

Fig. 10.—The orderly arrangement of the smooth muscle fibers encroaching on the narrow lumen is demonstrated. Hematoxylin and eosin, magnification × 300.

Serial sections were made longitudinally through the atriovenous junction of the pulmonary vein from the left lower lobe. These sections revealed severe stenosis rather than atresia (Fig. 9). This stenosis was due to loosely, but orderly, arranged longitudinal smooth muscle fibers encroaching on the lumen of the vein (Fig. 10). This lumen was quite tortuous, and in no place was it as much as 0.5 mm. in diameter. Tortuosity prevented tracing of this lumen in any single slide, and serial sections were necessary to observe the patency of the lumen. No exudate was noted, and there was no evidence of recent or old hemorrhage or thrombosis.

DISCUSSION

Extrapulmonary stenosis of the pulmonary veins is a rare congenital lesion. The case reported above is the only instance of such change in a series of 264 cases of congenital heart disease in the cardiac museum at Children's Hospital of Pittsburgh. A search of the literature has uncovered only three additional cases of congenital obstruction of the pulmonary veins.

Only one of these reported cases closely resembled the case considered in the present report. The case was reported by Reye.[6] It concerned an 8-year-old girl who was known to have periods of stupor, and who had a persistent elevated pulse rate. She died in congestive failure, and autopsy revealed cor pulmonale with right-sided endocardial thickening and atheromas in the large branches of the pulmonary artery. In this instance all veins entering the left atrium were stenotic. The stenosis was due to thickening of the venous walls by loose bundles of smooth muscle without evidence of inflammation or thrombosis.

A case reported by Emslie-Smith and associates[3] was that of a 14-year-old girl whose symptoms began with cyanosis when she was 2 months old. Cardiac catheterization had demonstrated a patent ductus arteriosus, and a higher pressure in the pulmonary artery than in the aorta. At autopsy the left lung was found to drain normally. Two pulmonary veins of normal external diameter emanated from the right lung. The superior right pulmonary vein was obstructed at its atrial termination by a membranous diaphragm containing two tiny openings that admitted only a very fine probe. The lower right pulmonary vein appeared to end blindly and did not communicate with the atrium or the superior vein. A venous shunt from the right lung to the systemic circuit was observed in the form of dilated and tortuous subpleural veins that converged to form a large leash that emptied into the azygous vein. A widely patent ductus arteriosus was present. Firmness and hemosiderosis present in the right lung were absent in the unobstructed left lung. The pulmonary arteries in both lungs were altered by atheromas without calcification or thrombosis. Microscopic appearance of pulmonary arterioles was not reported.

A third instance of congenital stenosis of pulmonary veins was reported by Andrews.[1] It was in a 3-year-old girl who also had tricuspid atresia and transposition of the great vessels. The left pulmonary veins were fibrous cords only 2 mm. in over-all diameter. They contained tiny endothelialized channels. Medial hypertrophy and intimal proliferation of arterioles and small arteries were noted in the fibrotic left lung. Fibrosis and vascular change were not present in the right lung.

Two of the three cases from the literature were complicated by additional congenital cardiac malformations, while the cases of Reye and the present authors were without other congenital cardiac defects. In the complicated cases the stenosis was caused by either atresia of veins or a membranous diaphragm. In the two uncomplicated cases there were similar stenosing cuffs of orderly, loose smooth muscle fibers lying within veins of normal external diameter at their atrial junctions. All veins were involved in one instance (Reye's case), while three of five were so affected in the other (the case reported in this paper).

Some observations on the anatomy of the uncomplicated cases are of special interest to the surgeon. The normal external diameter and insertion of the stenotic veins does not permit diagnosis by inspection in the cadaver. It is conceivable that variation in color and distensibility may suggest the stenosis when viewed during life. However, the loose smooth muscle forming the stenosing cuffs is rather soft and may not give sufficient resistance to permit diagnosis by palpation. It may be necessary to probe these veins in order to establish the existence of obstruction. The stenosing cuff begins at the atrial endocardium and is less than 1 cm. long. On the pulmonary side of this short stenotic segment the veins have normally formed walls. Excision of the obstruction, followed by anastomosis of the normal portions of the pulmonary veins to the left atrium, would seem to be anatomically feasible.

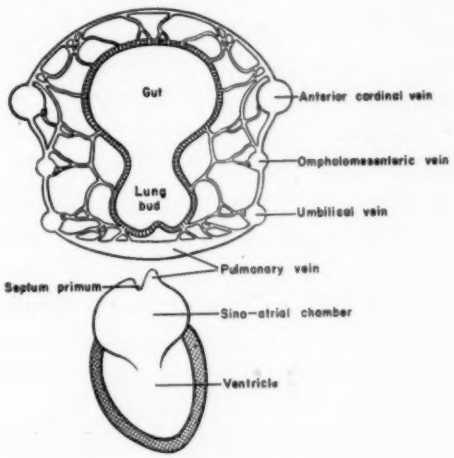

Fig. 11.—This diagram, modified after Hickie et al.,[4] illustrates the venous plexus shared by the foregut and lung buds. Drainage, at this stage, is to the anterior cardinal, vitelline, and umbilical veins. The outgrowth from the sinoatrial chamber will fuse with the plexus of veins in the region of the lung bud and establish drainage to the atrium.

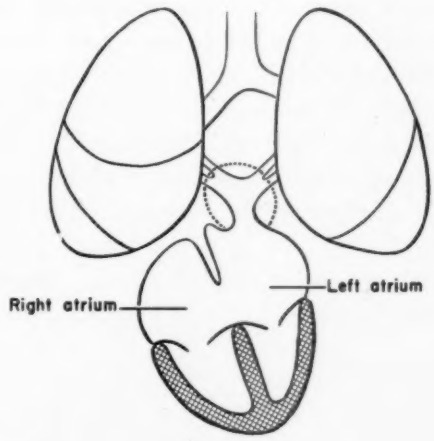

Fig. 12.—This diagram illustrates the pulmonary return through a common channel. The common pulmonary vein and its lobar branches, lying within the dotted lines, will be incorporated in the left atrium as growth progresses.

We agree with Reye[6] that the absence of inflammation, hemorrhage, and thrombosis and the orderliness of the stenosing tissue indicate a congenital malformation as the cause of this type of stenosis. This must occur in a stage of development after the formation of the pulmonary vein and after the disappearance of the pulmonary anastomoses with the anterior cardinal, vitelline, and umbilical veins (Fig. 11). Stenosis occurring before these anastomosing channels are obliterated would probably result in anomalous pulmonary venous connection to the systemic return by persistence of one of these channels. The common pulmonary vein is present in the 2-cm. embryo. It is slowly incorporated into the left atrium by a process of differential growth that is not quite complete in the 9-cm. embryo.[6] Incorporation of the branches of the pulmonary venous trunk by this growth process is the method by which the orifices of the pulmonary veins come to lie in their normal positions (Fig. 12). An overgrowth or failure of involution of smooth muscle in the terminal portion of the pulmonary veins could account for the stenosis. The superior positions of the veins from the lower lobes suggest an alteration in the incorporation of the venous trunk and its tributaries into the left atrium.

The changes that occur secondary to the venous obstruction are pulmonary hypertension and hyperemia, and some degree of shunting of pulmonary venous return to systemic veins via bronchial veins. These changes are reflected in the clinical course.

Anatomic changes related to pulmonary hypertension in the case reported here were the cor pulmonale and a generalized thickening of arteriolar walls. The involvement of unobstructed as well as obstructed lobes in the arteriolar hypertrophy in our case differs from the findings in a case of acquired (inflammatory) obstruction reported by Edwards and Burchell,[2] in which the single unobstructed lobe was not affected by arteriolar occlusive change present in the obstructed lobes. The occlusive change in their case of acquired pulmonary venous obstruction was interpreted as a protective mechanism to prevent excessive capillary congestion.

Capillary hyperemia, hemosiderosis, and focal fibrosis as described by Andrews[1] were present in the case herein reported; these changes were confined essentially to the obstructed lobes. The capillary hyperemia probably indicates increased capillary tension. Hypertension in the capillaries would help to explain the abundance of fibrin-containing fluid exudate in foci of inflammation noted in the obstructed right lower lobe, where but a minimum of acute cellular exudate was present. This fluid exudate, with accompanying small hemorrhages, blocked terminal bronchioles and might explain the severe respiratory distress suffered by this patient during minor respiratory infections. Healing of such inflammatory foci by organization could explain the patchy distribution of fibrosis in obstructed lobes.

SUMMARY

1. A case of congenital stenosis of the pulmonary veins is presented.
2. The brief literature on congenital pulmonary venous stenosis is reviewed.

Only one similar case was found. Two other reported cases of congenital stenosis were complicated by cardiac anomalies and presented different types of stenosing lesions.

3. The anatomy of this lesion with special reference to the possibility of surgical correction is discussed.

4. The secondary effects of pulmonary venous obstruction in this case are: pulmonary hypertension, hyperemia, edema, focal fibrosis, hemosiderosis, an unusual response to inflammation, and some shunting of pulmonary venous blood to the systemic return.

REFERENCES

1. Andrews, E. C., Jr.: Bull. Johns Hopkins Hospital. **100**:28, 1957.
2. Edwards, J. E., and Burchell, H. B.: Arch. Int. Med. **87**:372, 1951.
3. Emslie-Smith, D., Hill. I. G. W., and Lowe, K. G.: Brit. Heart J. **17**:79, 1955.
4. Hickie, J. B., Gimlette, T. M. D., and Bacon, A. P. C.: Brit. Heart J. **18**:365, 1956.
5. Nick, J.: Thoraxchirurgie **1**:387, 1953-54.
6. Reye, R. D. K.: Med. J. Australia **1**:801, 1951.

A Vector Study of the Delta Wave in "Nondelayed" Conduction

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In 1915, Wilson[1] described "a case in which vagus influenced the form of the ventricular complex of the electrocardiogram," that is, short P-R interval and long QRS duration were present in the classic limb leads. Subsequently, this became known, among other names, as the Wolff-Parkinson-White (WPW) syndrome because of the first comprehensive study by the corresponding authors,[2] or as the Wilson-Wolff-Parkinson-White (WWPW) syndrome in due honor of its originators.[3] The initial slurring of the R deflection has been designated as the delta wave.[4] But even though almost 200 papers on the subject have been accumulated, the cause of the delta wave remains obscure.

From a body of about 50 theories concerning its cause one may distinguish two basic ideas for the appearance of the delta wave: the impulse of the delta wave conducted through an accessory atrioventricular pathway; and the impulse of the delta wave conducted through the normal conductive system without the normal delay in the atrioventricular node.

Recent extensive, experimental work of Prinzmetal and associates[5] is in favor of the second idea. They were unable to produce this electrocardiographic syndrome in dogs when the bundle of His was cut. Therefore, until our knowledge of this is finally complete, it is at present reasonable to assume that the syndrome may be caused by an impulse traveling over the normal conductive system in the absence of a normal delay in the atrioventricular node. In other words, there is the existence of a "nondelayed" conduction.

In vector study of the electrocardiogram of "nondelayed" conduction one may distinguish a main vector of the delta wave, a main vector of the remaining QRS complex, and the angle defined by the two vectors. This paper concerns such studies in the RLF plane.

THE STUDY

Altogether, 50 limb lead electrocardiograms of 50 cases of "nondelayed" conduction were chosen from this laboratory. The P-R interval was 0.12 second or less; the QRS complex was 0.10 second or more with gradual initial slope and slurring, the delta wave. The P-J interval was either

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of normal duration or shorter. Variations have been excluded, such as short P-R interval with normal QRS duration, concertina effect, and others.[6,7] The Sanborn Viso-Cardiette was the recording instrument.

Of each electrocardiogram the delta wave vector,* the remaining QRS vector, and the angle between the two vectors were obtained in the circular system, derived from the Einthoven triangle by us previously.[8]

Fig. 1 shows the circular system. It consists of six concentric polarity circles representing, from within outward, the limb leads I, II, III, R, L, and F. Each polarity circle is composed of a positive semicircle (white), a negative semicircle (dotted), and two zero potential boundaries. Any vector residing in the positive semicircle will yield a positive deflection in the respective lead, any in the negative semicircle a negative deflection, and any coinciding with one boundary an isoelectric line or a transitional complex. This system divides the RLF plane into 24 directions with 15 degrees of angulation between them.

The electrocardiogram reproduced below the system in Fig. 1 was selected at random by way of example. The white arrow in the system indicates the delta wave vector, and the black arrow indicates the remaining QRS vector. The angle between the two vectors is seen to be 15 degrees.

The total data are presented in Table I. Tables II and III give, respectively, the directional incidence of the two vectors and the incidence of the various angles. Fig. 2 illustrates the directional incidence in percentage of the delta wave vector in the RLF plane. In Fig. 3, *A* illustrates the directional incidence in percentage of the remaining QRS vector, and *B* illustrates the incidence in percentage of the various angles.

The average delta wave vector was calculated to have an approximate direction of +20 degrees, and the average remaining QRS vector, a direction of +10 degrees. The average angle was about 30 degrees.

TABLE I. THE DELTA WAVE VECTOR (QRS′), THE REMAINING QRS VECTOR (QRS″), AND THE ANGLE BETWEEN THEM FROM EACH LIMB LEAD ELECTROCARDIOGRAM OF "NONDELAYED" CONDUCTION

ECG	QRS′ (DEGREES)	QRS″ (DEGREES)	ANGLE (DEGREES)	ECG	QRS′ (DEGREES)	QRS″ (DEGREES)	ANGLE (DEGREES)
1	+15	+15	0	26	+75	+75	0
2	+30	−15	45	27	+75	+45	30
3	−15	−45	30	28	+45	−45	90
4	+75	+75	0	29	−30	−45	15
5	+90	+105	15	30	+105	+90	15
6	−45	−45	0	31	−15	−15	0
7	−45	−75	30	32	0	+60	60
8	+15	−45	60	33	+45	−45	90
9	+75	+75	0	34	+105	+90	15
10	−75	−105	30	35	−30	−30	0
11	−45	0	45	36	+15	−75	90
12	−30	−60	30	37	+30	+15	15
13	0	−45	45	38	+75	+75	0
14	+15	+15	0	39	+45	0	45
15	+45	+60	15	40	−30	−30	0
16	+60	+45	15	41	−15	+45	60
17	−15	+75	90	42	−15	0	15
18	+15	0	15	43	+15	−15	30
19	+15	+45	30	44	−30	−30	0
20	+15	+30	15	45	−15	−30	15
21	+30	+75	45	46	+75	+75	0
22	+15	−15	30	47	+45	0	45
23	+15	−15	30	48	+15	+45	30
24	+15	−15	30	49	−30	−75	45
25	+60	+45	15	50	+15	+15	0

*In this paper it means direction only, no magnitude is concerned.

TABLE II. THE DIRECTIONAL INCIDENCE OF QRS′ AND QRS″ IN THE RLF PLANE

DIRECTIONS (DEGREES)	QRS′ (DEGREES)	QRS″ (DEGREES)
−90		1
−75		3
−60	1	1
−45	3	7
−30	6	4
−15	6	6
0	2	5
+15	13	4
+30	3	1
+45	5	6
+60	2	2
+75	6	7
+90	1	2
+105	2	1
	50	50

TABLE III. THE ANGULAR INCIDENCE IN THE RLF PLANE

ANGLES (DEGREES)	ELECTROCARDIOGRAMS
0	13
15	12
30	11
45	7
60	3
90	4
	50

DISCUSSION

In slow motion cinematography, Prinzmetal and associates[5] studied in great detail the myocardial kinetics of the exposed dog heart. By means of a combined cinemato-electrocardiographic technique they were able to demonstrate a premature, weak, localized myocardial contraction associated with the inscription of the experimentally induced delta wave, and a subsequently normal contraction of the remaining ventricular musculature with that of the rest of the QRS. Their experimental data have been utilized to explain the clinical findings. We were of the opinion that the vector of the delta wave could be used to indicate the site of the premature, localized contraction.

Fig. 2 illustrates the directional incidence in percentage of the delta wave vector. These vectors all reside at the left half of the RLF plane. If indication could be made from the above finding as to the site of the premature, localized contraction, such a site would be an area of the ventricular wall facing the left half of the RLF plane. The average delta wave vector was calculated to be +20

degrees. However, this could not be the true direction. When volume conductor property and lead vector projection were considered,[9] we found that the corresponding true direction would be most likely 0 degrees. In other words, the frequent site of the premature, localized contraction would be approximately the left basal ventricular wall of either ventricle. Furthermore, one might postulate that in "nondelayed" conduction the fibers in the specific conductive system involved were those that innervate preferably the above-described regions.

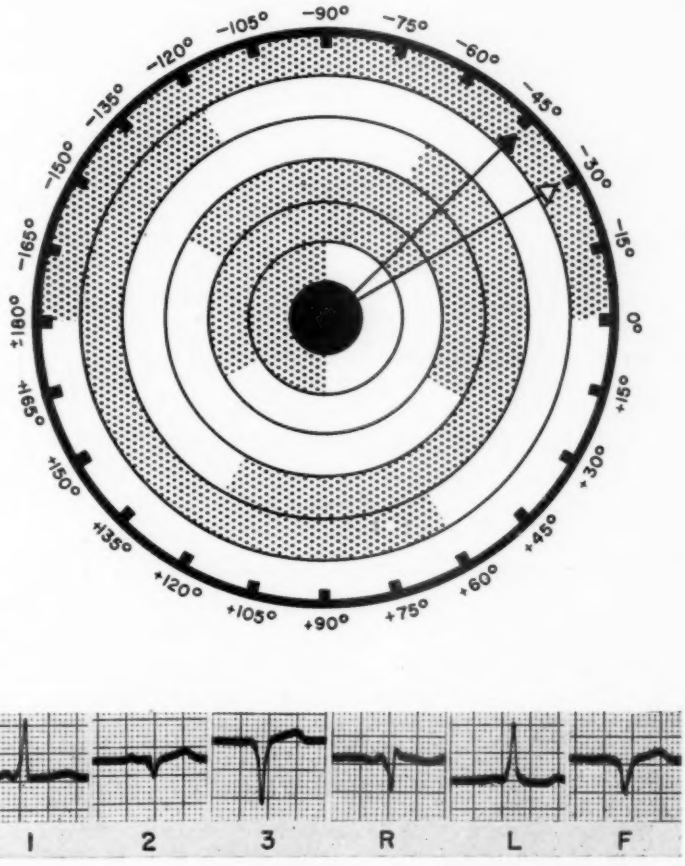

Fig. 1.—The circular system, and a limb lead electrocardiogram of "nondelayed" conduction.

Fig. 3, *A* illustrates the directional incidence in percentage of the remaining QRS vector. The curve resembles that obtained from electrocardiograms of left ventricular hypertrophy.[10] The average remaining QRS vector was +10 degrees. Therefore, a leftward tendency of the remaining QRS activation should be admitted. Its cause is unknown. The average angle was narrow, about 30 degrees, although individually it could be as large as 90 degrees (Fig. 3, *B*).

Until one understands completely the cause of this electrocardiographic syndrome, it is at present reasonable to assume that the cause is an impulse traveling over the normal conductive system in the absence of a normal delay

in the atrioventricular node. This was originally called the accelerated conduction.[5] However, in view of the fact that the assumption was the absence of a delay and not the presence of an acceleration, the term "nondelayed conduction" therefore appears to be preferable.

Finally, it is noteworthy to mention that most recently Hejtmancik and Herrmann[11] studied the largest series thus far of "nondelayed" conduction and found a high incidence among psychopathic patients. This might be considered

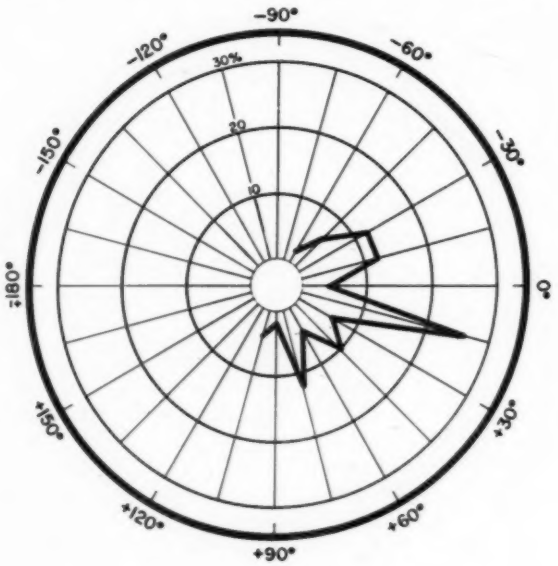

Fig. 2.—The directional incidence in percentage of the delta wave vector in the RLF plane.

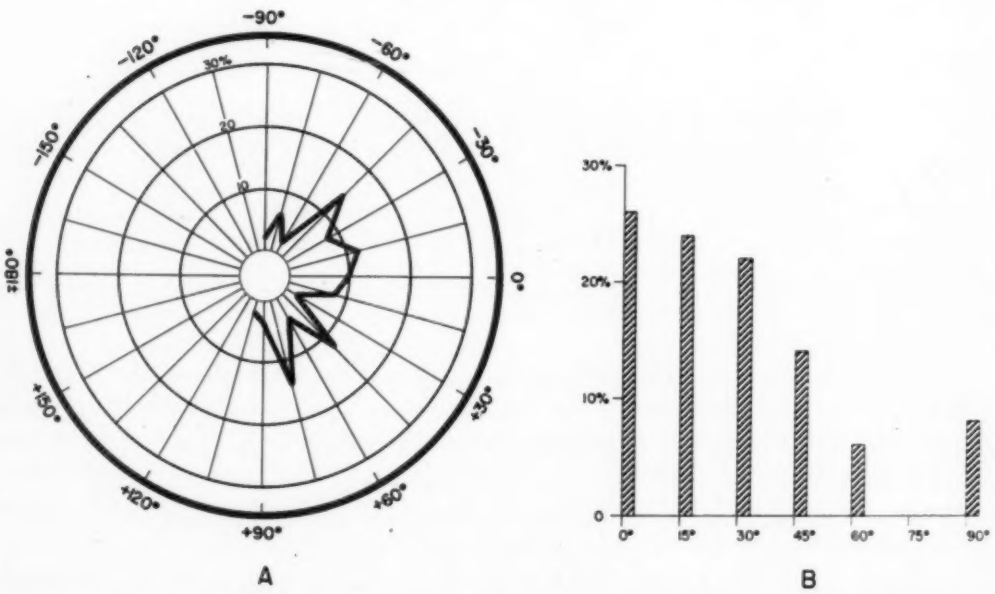

Fig. 3.—*A*, The directional incidence in percentage of remaining QRS vector in the RLF plane. *B*, The angular incidence in percentage in the RLF plane.

as emphasizing a possible neurogenic origin of the disorder, in agreement with Wilson's observation of the vagus influence in the first study of this disorder written over 40 years ago.[1]

SUMMARY

1. At present, the electrocardiographic syndrome discussed could be adequately described as a "nondelayed" conduction.

2. The directional incidence of the delta wave vector and remaining QRS vector, as well as the angular incidence between them at the RLF plane, were studied. The study was based on 50 limb lead electrocardiograms of "nondelayed" conduction.

3. The left basal ventricular wall of either ventricle may possibly be the frequent site of the premature, weak, localized contraction associated with the delta wave vector.

4. A leftward tendency of the remaining QRS activation was observed.

ADDENDUM

After this study had been completed, there appeared in the literature a paper concerning the "ventricular precontracting area in the Wolff-Parkinson-White syndrome, demonstrated in man" by means of a specific roentgenkymographic technique.[12] In that paper the site of the premature, localized ventricular contraction was compatible with that suggested in the present study from an analysis of the delta wave vector in the RLF plane.

REFERENCES

1. Wilson, F. N.: Arch. Int. Med. **16**:1008, 1915.
2. Wolff, L., Parkinson, J., and White, P. D.: Am. Heart J. **5**:685, 1930.
3. Herrmann, G. R.: A Synopsis of Diseases of the Heart and Arteries, St. Louis, 1936, The C. V. Mosby Company.
4. Öhnell, R. F.: Pre-Excitation—A Cardiac Abnormality, Stockholm, 1944, P. A. Norstedt & Soner. (Acta med. scandinav., Supp., **152**:1, 1944.)
5. Prinzmetal, M., Kennamer, R., Corday, E., Osborne, J. A., Fields, J., and Smith, L. A.: Accelerated Conduction, New York, 1952, Grune & Stratton.
6. Fox, T. T.: Am. J. M. Sc. **209**:199, 1945.
7. Burch, G. E., and Kimball, J. L.: Am. Heart J. **32**:560, 1946.
8. Zao, Z. Z.: Cardiologia **29**:36, 1956.
9. Zao, Z. Z., Hejtmancik, M. R., and Herrmann, G. R.: Circulation **14**:1023, 1956.
10. Zao, Z. Z., Herrmann, G. R., and Hejtmancik, M. R.: Am. Heart J. **56**:65, 1958.
11. Hejtmancik, M. R., and Herrmann, G. R.: Am. Heart J. **54**:708, 1957.
12. Bandiera, G., and Antognetti, P. F.: Circulation **17**:225, 1958.

Acute Myocardial Injury During Cardiopulmonary Bypass

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The following report describes electrocardiographic changes which resulted from obstruction of the right coronary artery in the course of an operation on the heart.

CASE REPORT

The patient was a 36-year-old woman with an atrial septal defect. The pulmonary arterial pressure was normal. Prior to her admission to hospital for closure of the defect she had been receiving digitalis therapy, and this was continued. The cardiopulmonary bypass, using a Lillehei-DeWall oxygenator, lasted 23 minutes; during the bypass the aorta was not clamped. Except for the electrocardiographic changes, which will be described in detail, the operative course was uneventful.

Electrocardiographic Changes.—In the preoperative electrocardiogram (not shown), sinus rhythm was present and the effect of digitalis was apparent. Immediately prior to the start of extracorporeal circulation a nodal rhythm was present, but both the R and T waves, and the S-T segments were the same as those seen on the preoperative tracing.

Progressive elevation of the R-ST segment began shortly after complete bypass was established, and gradually increased for 15 minutes (Fig. 1). At this time the R and T waves formed a single large complex. It was then discovered that a retractor placed in the right atrium was compressing the right coronary artery in the atrioventricular groove. Between 15 and 19 minutes after the start of the bypass the position of the retractor was changed, resulting in regression of the abnormal pattern of the electrocardiogram (Fig. 1: *19'36"* and *22'24"*).

The last electrocardiogram, recorded 40 minutes after completion of the bypass, was similar to the preoperative tracing: the effect of digitalis was again apparent and sinus rhythm had been re-established (Fig. 1: *63'*).

DISCUSSION

In our experience with more than 60 cardiopulmonary bypasses, electrocardiographic changes of the type described here have been seen only in this one patient. There can be no doubt that the changes were induced by interference with the myocardial blood supply, and the progression and regression of the electrocardiographic abnormalities preclude a diagnosis of bundle branch block.

Elevation of the RS-T segment with upright T waves accompanies injury to the myocardium (Goldberger[1]), and this was the pattern seen here. Kownacki

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and Kownacki[2] demonstrated in dogs that partial constriction of the circumflex coronary artery gave rise to inversion of the T wave. Further constriction of this artery was followed by elevation of the RS-T segment, the terminal portion of the T wave becoming positive. Kownacki and Kownacki did not illustrate regression of these changes to normal, but the fact that this can occur within minutes of restoration of the circulation has been demonstrated by Bayley, La Due and York.[3]

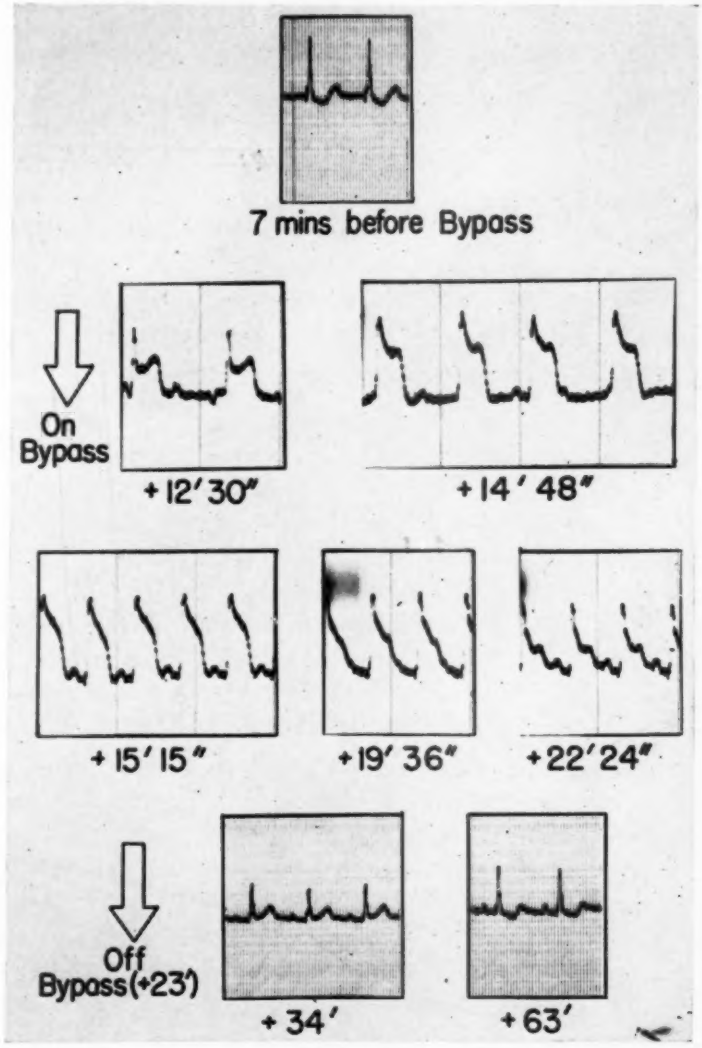

Fig. 1.—See text.

Blumgart, Gilligan and Schlesinger[4] have found that coronary arterial occlusion lasting 20 minutes or more is likely to be followed by permanent myocardial damage. In our patient, occlusion lasted less than 20 minutes and the pattern of the electrocardiogram returned to the preoperative form. For these reasons we believe that no permanent damage resulted from arterial obstruction.

SUMMARY

Changes in the pattern of the electrocardiogram following inadvertent obstruction of the right coronary artery during cardiopulmonary bypass are described in a patient with an atrial septal defect.

REFERENCES

1. Goldberger, E.: Brit. Heart J. **12**:141, 1950.
2. Kownacki, V. P., and Kownacki, R. J.: Am. Heart J. **55**:535, 1958.
3. Bayley, R. H., La Due, J. S., and York, D. J.: Am. Heart J. **27**:657, 1944.
4. Blumgart, H. L., Gilligan, D. R., and Schlesinger, M. J.: Am. Heart J. **22**:374, 1941.

An Electrocardiographic Demonstration of Atrial Dissociation

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The purpose of this paper is to present electrocardiograms which demonstrate atrial dissociation. The patient repeatedly experienced episodes of ventricular standstill, and during one episode an electrocardiographic strip was obtained in which two distinct sets of P waves could be clearly defined (Fig. 1). At a subsequent moment the two P waves fused into a single, widened, notched P wave (Fig. 2), indicating that atrial dissociation was no longer present but that some degree of intra-atrial block remained.

DISCUSSION

It has recently been emphasized that a distinction should be made between true dissociation of the atria and intra-atrial block.[1] The former term indicates either that the atria are being activated independently or that a portion of one atrium is independent of the bulk of atrial tissue, whereas the latter term applies when conduction of electrical activity throughout the atria is prolonged with widening or notching of the P waves.

An extensive review of previously reported cases has been ably done by others.[1,2] Some of these cases seem to demonstrate intra-atrial dissociation, while others are questionable. The first case of Bay and Adams[3] is convincing but their second and third cases are suspect as artifacts. The case presented by Hertz[4] also seems acceptable, although it has been questioned by others.[1,2] Deitz, Marriott, Fletcher, and Bellet[1] recently presented three cases. In the first case artifact seems to be a reasonable possibility. The second and third cases are convincing. The second case is interesting in that it demonstrates an increase in the rate of one atrial focus until fibrillatory waves resulted uniatrially.

The tracings presented in this paper are of interest because they seem to represent a clear case of atrial dissociation, and because no previous example of atrial dissociation occurring during prolonged ventricular standstill could be found.

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Fig. 1.—A continuous strip of Lead II taken during prolonged ventricular standstill reveals two independent sets of P waves. These are designated P_1 and P_2. The first eight waves have a notched or broad contour. In the ninth wave, P_1 and P_2 are more exactly superimposed, giving the wave a "peaked" appearance. The next eight waves have this same "peaked" contour. The next to the last complex of the first strip shows P_2 moving ahead of P_1. Throughout the next three lines, P_1 and P_2 are completely dissociated. When P_1 and P_2 are exactly superimposed, the wave again has a sharp "peaked" appearance; when they are superimposed less exactly, the wave has a broad or notched contour similar to the contour of the P wave in Fig. 2. The periodic high frequency vibrations (*T*) noted throughout the tracing represent muscular tremor due to the seizure associated with ventricular standstill. At times, P_2 is obscured by these vibrations. The rate of P_1 can be seen to vary between 60 and 100 per minute. P_2 occurs at about 44 per minute.

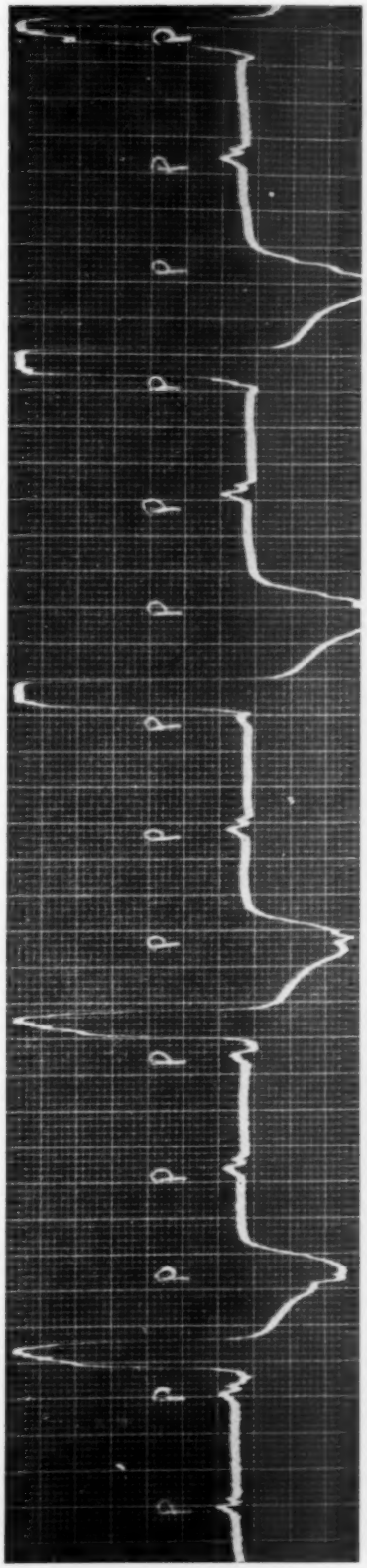

Fig. 2.—A continuous strip of Lead III reveals complete atrioventricular dissociation with an idioventricular pacemaker. The P waves have a constant notched contour resulting from the fusion of P_1 and P_2. Atrial dissociation is no longer present but some degree of intra-atrial block remains.

SUMMARY

Electrocardiograms revealing atrial dissociation occurring during an episode of ventricular standstill are presented and described.

REFERENCES

1. Deitz, G. W., III, Marriott, H. J. L., Fletcher, E., and Bellet, S.: Circulation **15**:883, 1957.
2. Decherd, G. M., Jr., Ruskin, A., and Brindley, P.: AM. HEART J. **31**:352, 1946.
3. Bay, E. B., and Adams, W.: AM. HEART J. **7**:759, 1932.
4. Hertz, J.: Acta med. scandinav. **101**:409, 1939.

Correlative Observations on the Electrocardiogram and Morphology of the Heart of the Florida Manatee

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Over the years there has been considerable interest in the comparative electrocardiography of large mammals. The elephant[1,2] and whale[3] have received principal attention because of their extreme size, and instructive data have been published on the anatomy of the heart,[3,4] as well as standard electrocardiographic measurements in these animals. It is an interesting and apparently overlooked fact that occupying a position midway between the Pachydermata and Cetacea in the phylogenetic scale[5,6] is an order of mammals, facing extinction, which possesses a unique anatomic peculiarity of the heart which makes them not only of special interest to completing the information on one group of large mammals but also adds a note to electrocardiography in general. The Sirenia are represented by two distinct genera: the Manatee which ranges the Atlantic coasts of tropical and subtropical America, the West Coast of Africa, and the East Coast of Africa north to Mozambique; and the Dugong which is found on the shores of the South Pacific and Indian Oceans. Anatomic papers[6-8] many years ago called particular attention to the bifid ventricles in the hearts of these animals, and Steller described this peculiarity in the now extinct genus which bears his name. No note appears to have been taken of possibly unusual functional properties which this structural feature might engender. Particularly, as regards the electrocardiogram, it would be interesting to know if it were possible with bifid ventricles to record a "septal" Q wave; or if there were any peculiarity in the morphology of the QRS complex, since the muscle bundles must show considerable deviation from the normal mammalian pattern, particularly in the region of the apex.

METHODS

The electrocardiogram was recorded from a male Florida manatee, *Trichechus latirostris* (Harlan), six years of age and weighing 1,100 pounds, which had been maintained in captivity for several years. When the water was removed from the aquarium, the animal was left resting

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ventral side down, helpless on the bottom, but since this was a frequent procedure associated with cleaning, he had apparently grown accustomed to it and exhibited no agitation or restlessness. Large surface electrodes were attached to the tail and front flippers, and the three standard leads of the electrocardiogram were recorded with a direct-writing portable instrument.

The anatomic studies were made on a large, mature, male specimen which washed up dead on the Florida shore. No obvious cause of death was apparent, and the complete dissection revealed nothing further to indicate any gross abnormality. Body weight was estimated by several observers as between 1,500 and 2,000 pounds. Fig. 1 shows the dissected carcass and the position of the heart in the body shell. The heart was fixed in 10 per cent Formalin, and the complete dissection was carried out several weeks later in the laboratory.

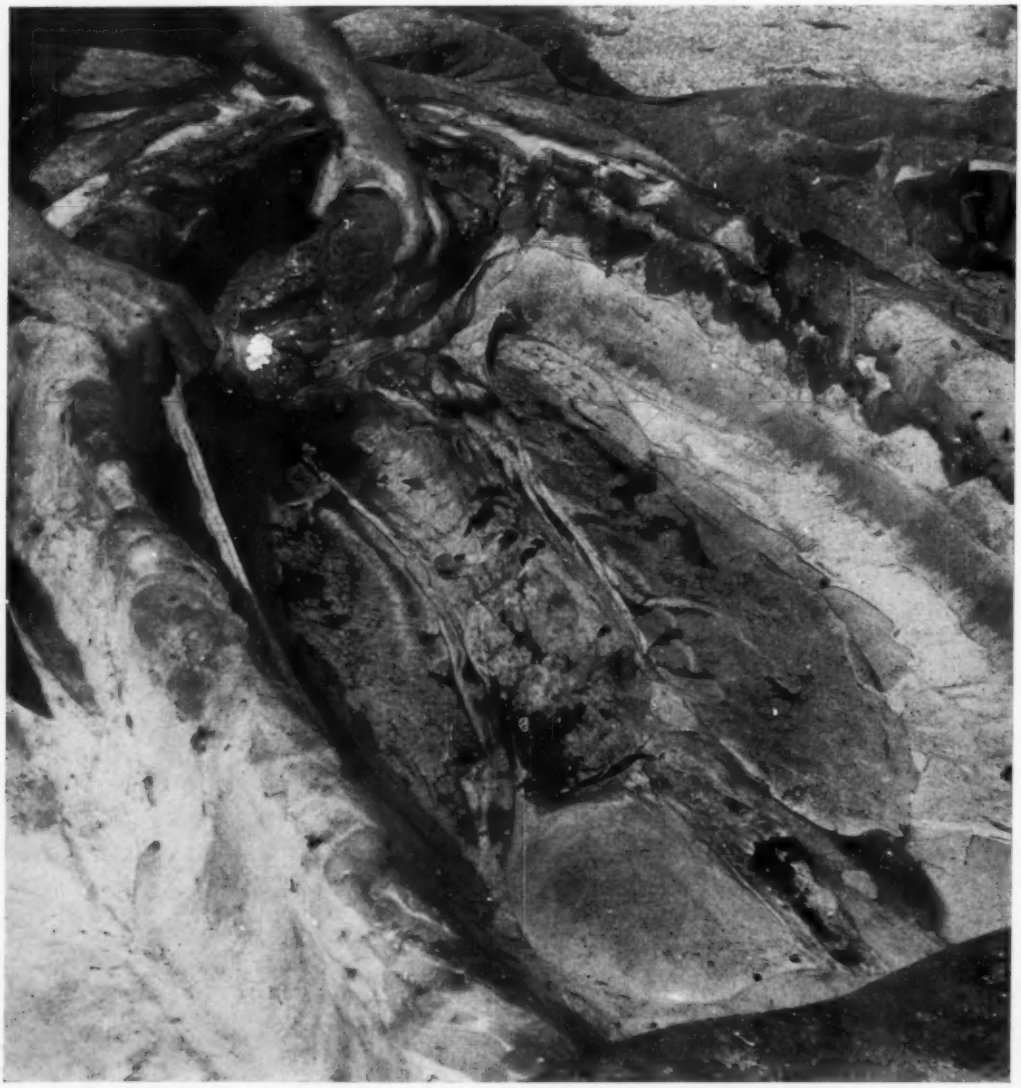

Fig. 1.—Carcass of mature manatee with heart and lungs exposed through ventral midline incision. Abdominal viscera have been removed. The heart is high in the thorax; the left ventricle is held in the left hand. The lungs are long, narrow structures lying dorsally well below the heart and behind the abdominal viscera but separated from them by the diaphragm, a portion of which is reflected by the right hand.

RESULTS AND DISCUSSION

The heart of the animal which was dissected weighed only 810 grams, an extraordinarily small value considered as per unit of total body weight when compared to this ratio for other mammals. The low resting metabolism and sluggish nature of the manatee probably provide sufficient reason. The bifid nature of the ventricles was readily apparent, the cleft extending about halfway from apex to base. The region near the base where the ventricles were in approximation contained much fat, which, on removal, revealed no superficial muscle bundles common to the two ventricles in this area. In fact, although the medial walls were somewhat adherent, the approximating tissue was almost all fibrous, and with careful blunt dissection the two ventricles could be separated up to the auriculoventricular junction without damaging any muscle fibers except at the extreme base where a few deep fibers appeared to be common to both ventricles.

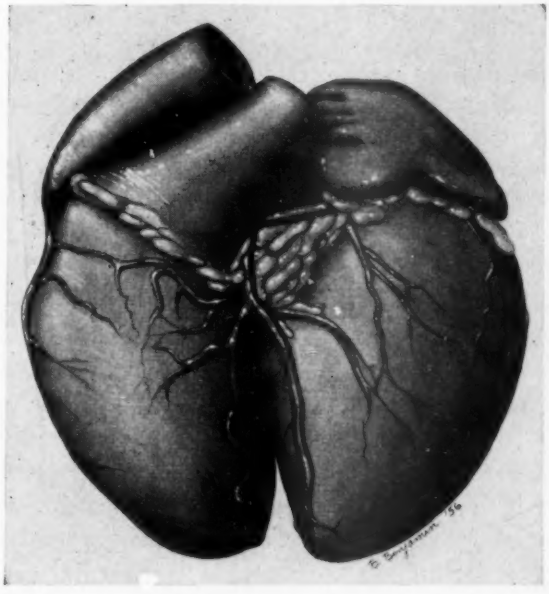

Fig. 2.—Artist's sketch of manatee heart seen from the front. Right atrium is entirely posterior.

These arose posteriorly from the basal portion of the left ventricle, spiraled in a clockwise direction (viewed from the apex) primarily around the aorta, but a few fibers crossed, deep in the sulcus, to the right ventricle. Fig. 2 is a drawing of this heart with the superficial fat removed. Nothing from the gross appearance adds significantly to the descriptions in the old literature except perhaps relative to the unique relations of the muscle bundles and a note on the division of the anterior descending coronary artery resulting in a separate branch to the medial wall of each ventricle (see illustration). Internally, the specialized conduction tissue was clearly visualized as a pale gray band running along the medial wall of each ventricle, and on histologic examination revealed the expected characteristics. The aorta and pulmonary artery had thick walls, and no atherosclerotic plaques or calcifications were noted.

Standard Lead I of the electrocardiogram was adequately recorded (Fig. 3) and revealed nothing unusual in general morphology. The P wave was poorly defined but probably biphasic; the ventricular complex was characterized by a small R wave and a prominent S wave, the latter showing a very small notch on the return to base line. The S-T segment was isoelectric and the T wave upright.

TABLE I. MEASUREMENTS OF MATURE MANATEE HEART

Weight	810 Gm.
Thickness of left ventricular wall	16.0 mm.
Thickness of right ventricular wall	3.0 mm.
Diameter of pulmonary artery	3.2 cm.
Diameter of aorta	2.9 cm.
Length of left ventricle	11.0 cm.
Length of right ventricle	7.5 cm.

TABLE II. ELECTROCARDIOGRAPHIC AND ANATOMIC DATA ON THREE CLOSELY RELATED MAMMALS

SPECIES	HEART RATE	P-R	QRS	Q-T	HEART WEIGHT/ BODY WEIGHT RATIO
Whale[3]	12–24	0.28–0.41	0.9–0.12	——	0.0051
Manatee	75	0.26	0.10	0.44	0.0010
Elephant[1,2]	40	0.3	0.16	0.65	0.0044

The measurements which are summarized in Table II include for comparison those from the most closely related large mammals, and indicate common features of a long P-R interval, normal QRS duration, and long Q-T interval by human standards. It is particularly interesting that the ventricular complex contains a small initial deflection which would be regarded by some as being of "septal" origin; yet, it is difficult to conceive any significant activation of this heart across the very short portion near the base where the two ventricles appear to have a common wall. In this region the muscles of the two ventricles are very readily separated, there being considerable connective tissue and fat between them. On the other hand, the bundle of His has divided in this region and there may well be an early inequality in rate of invasion of these paths in the two ventricles which could establish momentary vectors, the resultant of which might produce an early transitory deflection.[9] If the spread along each medial wall were radially, from specialized tissue out through ventricular muscle, the greater mass on the left would make this a predominantly left ventricular effect.[10] In the manatee heart, without full septum, the initial ventricular deflection so generated would be analogous to that commonly called "septal." Even in the usual mammalian heart with full septum, the structure is primarily left ventricle, and the excitatory process during early invasion of the ventricles may be like that in the Sirenian heart.

Furthermore, the absence of any prominent abnormality in the QRS pattern is pertinent to an evaluation of the significance of the muscle bundle systems as conduction systems in the ventricle. Robb has suggested that the excitatory process in the mammalian ventricle may cross the interventricular groove and then run parallel to the fibers of the muscle bundles,[11] and has further presented experimental evidence which suggests that interference with these bundles results in distinct electrocardiographic patterns,[12] e.g., a cut of the superficial bulbo-spiral muscle resulted in an alteration which looked like a "coronary pattern."[13]

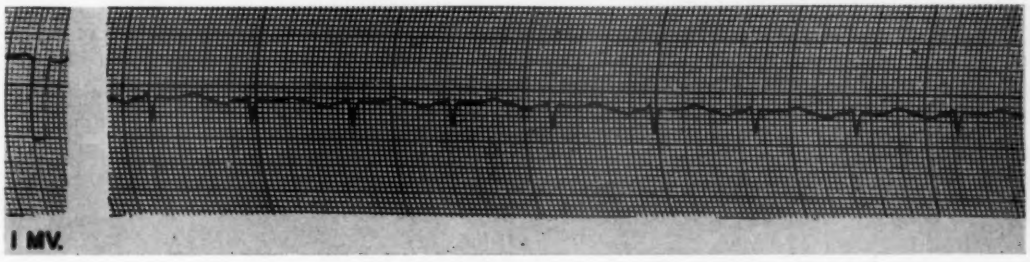

Fig. 3.—Standard Lead I of electrocardiogram. Paper speed 25 mm. per second.

While a complete description of the muscle bundle system in the Sirenian heart has not been attempted, it is clear that the bifid nature of the ventricles introduces a situation in which the usual pattern seen in the mammalian heart cannot exist. The superficial bulbo-spiral and the superficial sino-spiral muscles are common to both ventricles in the human heart, coursing around the apex, but this cannot be true in a heart with two "apices." Yet in spite of these gross differences the ECG looks "normal," and may thus provide an indirect but interesting bit of evidence which stands to question the importance of the muscle bundles as significant determinants of the morphology of the ECG.

SUMMARY AND CONCLUSIONS

1. The Sirenia, an order of large mammals midway between the Pachydermata and Cetacea in the phylogenetic scale, are of interest not only for the completion of electrocardiographic information in this mammalian group, but also because a unique anatomic feature of their heart, viz., bifid ventricles, introduces the possibility of unusual electrocardiographic contour.

2. The electrocardiogram was entirely similar to the records published for the manatee's two closest relatives, the elephant and the whale. Nothing distinctive was apparent.

3. The gross appearance of the heart is described briefly. The heart weight, expressed as a ratio of total body weight, is the smallest recorded for any mammal.

The author gratefully acknowledges the kind cooperation of Dr. Perry Sperber and his staff at the Sea Zoo, South Daytona Beach, Fla., who made this study possible.

REFERENCES

1. Forbes, A., Cobb, S., and Cattell, McK.: Am. J. Physiol. 55:385, 1921.

2. White, P. D., Jenks, J. L., and Benedict, F. G.: Am. Heart J. **16**:744, 1938.
3. King, R. L., Jenks, J. L., and White, P. D.: Circulation **8**:387, 1953.
4. King, R. L., Burwell, C. S., and White, P. D.: Am. Heart J. **16**:734, 1938.
5. Brown, A. E.: Am. Naturalist **12**:291, 1878.
6. Murie, J.: Tr. Zool. Soc. (London) **8**:127, 1870.
7. Owen: Proc. Zool. Soc. (London), Part VI, p. 28, 1838.
8. Garrod, A. H.: Tr. Zool. Soc. (London) **10**:137, 1878.
9. Bayley, R. H.: J. Trop. Med. and Hygiene **41**:144, 1938.
10. Sodi-Pallares, D., Rodriguez, M. I., Chait, L. O., and Zuckermann, R.: Am. Heart J. **41**:569, 1951.
11. Robb, J. S., and Robb, R. C.: Am. J. Physiol. **115**:43, 1936.
12. Robb, J. S., and Robb, R. C.: Am. Heart J. **23**:455, 1942.
13. Robb, J. S., Easby, M., and Hiss, J. G. F.: Am. J. Med. Sc. **188**:835, 1934.

INDEX TO VOLUME 56

Author Index

A

AARSETH, SVERRE, AND LANGE, HENRIK F. The influence of anticoagulant therapy on the occurrence of cardiac rupture and hemopericardium following heart infarction. I. A study of 89 cases of hemopericardium (81 of them cardiac ruptures), 250

——. (*See* Lange and Aarseth), 257

ANDERSON, ALBERT, AND RUBIN, IRA L. Simultaneous atrial flutter and ventricular tachycardia, 299

ANGELAKOS, E. T., TORRES, J., AND DRISCOLL, R. Ouabain on the hypothermic dog heart, 458

ANGLE, WILLIAM D. Myocardial infarction in the Wolff-Parkinson-White syndrome: a method of vector analysis of ECG changes, 36

ARANDA, S. (*See* Espino-Vela, et al.), 856

ARAVANIS, CHRIST, AVGOUSTAKIS, STAVROS, AND MICHAELIDES, GEORGE. Pulseless disease: report of a case, 126

AVGOUSTAKIS, STAVROS. (*See* Aravanis, et al.), 126

AZAN, LUIS. (*See* Castellanos, et al.), 562

B

BACANER, MARVIN. The occurrence of a rapid ventricular rate during atrial fibrillation as a paradoxical manifestation of digitalis intoxication, 685

BAER, DANIEL M., OSBORN, JOHN J., PERKINS, HERBERT A., MELROSE, DENIS G., NORMAN, ALAN, AND GERBODE, FRANK. Serum electrolyte observations following extracorporeal circulation, 652

BALAGUER-VINTRÓ, I. (*See* Torner-Soler, et al.), 425

BALL, MICHAEL F., AND PIPBERGER, HUBERT V. The normal spatial QRS-T angle of the orthogonal vectorcardiogram, 611

BANNERJI, K. (*See* Sanghvi, et al.), 79

BARBATO, ENNIO, FUJIOKA, TOSHYASU, DEBES, ANTONIO CARLOS, PILEGGI, FULVIO, FILHO, CELESTINO BOURROUL, SILVA, PAULO DE PAULA E, AND DÉCOURT, LUIZ V. Study of the sequence of ventricular activation and the QRS complex of the pathologic human heart, using direct epicardial leads, 340

BARNETT, A. J., AND WAGNER, G. R. Severe orthostatic hypotension: case report and description of response to sympatheticomimetic drugs, 412

BARRERA, FRANK. (*See* Castillo and Barrera), 769

BATSON, HUGH M. (*See* Birchall, et al.), 616

BAUERSFELD, S. RICHARD. (*See* Sherman, et al.), 908

BEARD, HALLARD W., AND THOMPSON, ROBERT G. Aneurysm of the ascending aorta caused by congenital syphilis, 313

BELLET, SAMUEL. Recent advances in the treatment of cardiac arrhythmias, 479

BIRCHALL, ROBERT, BATSON, HUGH, M., AND MOORE, CHARLES B. Hypertension due to unilateral renal arterial obstruction: preliminary observations on the contribution of differential renal clearance studies, 616

BLACKARD, EMBREE. (*See* Hurst and Blackard), 159

BLUMENFELD, SERGE. (*See* Scherf, et al.), 236

BODROGI, GEORGE. Ballistocardiographic findings on the J wave, 95

BOYD, THOMAS. (*See* Carleton and Boyd), 136

BRAUN, K. (*See* Rosenberg, et al.), 486

BRAVEMAN, WARREN S. (*See* Hollister, et al.), 629

BRODY, DANIEL A., AND COPELAND, G. DANIEL. Electrocardiographic cancellation: some observations concerning the "nondipolar" fraction of precordial electrocardiograms, 381

BURCH, GEORGE E. (*See* Hibbs, Burch, and Phillips), 662

BURGER, H. C., AND VAANE, J. P. A criterion characterizing the orientation of a vectorcardiogram in space, 29

C

CALDWELL, M. JUNE, AND PRIEST, EDWARD M. A different concept of prothrombin time control for anticoagulative therapy, 737

CALVIÑO, JOSÉ M. (*See* Castellanos, et. al.), 562

CARLETON, RICHARD A., AND BOYD, THOMAS. Traumatic laceration of the anterior descending coronary artery treated by ligation without myocardial infarction: report of a case with review of the literature, 136

CARRASCO-AZEMAR, J. (*See* Torner-Soler, et al.), 425

CASTELLANOS, AGUSTIN, JR., AZAN, LUIS, AND CALVIÑO, JOSÉ M. Dissociation with interference between pacemakers located within the A-V conducting system, 562

CASTER, W. O., GARAMELLA, J. J., VELOSO, A., AND NAIDU, R. Effect of acute coronary occlusion upon the movement of Evans blue dye into different areas of pig heart muscle, 658

CASTILLO, PEDRO A., AND BARRERA, FRANK. Human hypertension due to thrombotic occlusion of both renal arteries: report of a case "cured" by surgical removal of the thrombus, 769
COHEN, BURTON D. (*See* Hollister, et al.), 629
——. (*See* Spritz, et al.), 715
COMESAÑA, FRANCISCO. (*See* Nava, et al.), 598
COPELAND, G. DANIEL, AND STERN, THOMAS N. Wenckebach periods in pregnancy and puerperium, 291
——. (*See* Brody and Copeland), 381
COSSIO, PEDRO. The treatment of angina pectoris and other muscular pain due to ischemia with iproniazid and isoniazid, 113
CREVASSE, LAMAR, AND LOGUE, R. BRUCE. Valvular pulmonic stenosis: auscultatory and phonocardiographic characteristics, 898
CUPP, C. M., WOOLVIN, S. C., AND INMON, T. W. Chaotic heart due to metastatic synovioma, 695

D

DAMMIN, GUSTAVE J. (*See* Gill, et al.), 878
DASGUPTA, K. (*See* Larks and Dasgupta), 701
DAVIS, EARLE R. (*See* Fisher and Davis), 537, 553
DAVIS, LAWRENCE A. (*See* Leight and Davis), 129
DEBES, ANTONIO CARLOS. (*See* Barbato, et al.), 340
DÉCOURT, LUIZ V. (*See* Barbato, et al.), 340
DICK, H. LENOX H., MCCAWLEY, ELTON L., VOISS, DANIEL V., AND KRUEGER, JAMES D. Electrocardiographic evaluation studies on quinidine-induced changes of myocardial conduction, 396
——. (*See* McCawley, et al.), 405
DICKENS, JANET, AND GOLDBERG, HARRY. Correlation of the precordial and endocardial ventricular electrocardiogram, 8
—— and ——. The endocardial lead in complete right bundle branch block, 372
DIMOND, E. GREY, AND HAYES, WILLIAM L. An electrocardiographic demonstration of atrial dissociation, 929
DOUMA, J. H. (*See* Feer, et al.), 642
DRAKE, E. H. (*See* Kavanagh-Gray and Drake), 143
DRISCOLL, R. (*See* Angelakos, et al.), 458
DUCHOSAL, PIERRE W. Vectorcardiography, 1

E

ECHEVARRÍA, MAX. (*See* Peñaloza, et al.), 493
EDWARDS, JESSE E. (*See* Wakai and Edwards), 779
ENTERLINE, H. T. (*See* Stocker and Enterline), 51
ESCUDERO, JORGE, AND MCDEVITT, ELLEN. The electrocardiogram in scleroderma: analysis of 60 cases and review of the literature, 846
ESPINO-VELA, J., PORTILLO, B., RUBIO, V., AND ARANDA, S. Combined auricular and ventricular septal defects: a study of five cases with postmortem confirmation in three, 856
ESPINO-VELA—Cont'd
EULER, U. S. VON. Some aspects of the role of noradrenaline and adrenaline in circulation, 469

F

FEER, Y. VAN DER, DOUMA, J. H., AND KLIP, W. Cardiac output measurement by the injection method without arterial sampling, 642
FILHO, CELESTINO BOURROUL. (*See* Barbato, et al.), 340
FISHER, EDWIN R., AND DAVIS, EARLE R. Myocarditis with endocardial elastomyofibrosis (EEMF), 537
——, and ——. Observations concerning the pathogenesis of endocardial thickening in the adult heart, 553
FISHLEDER, BERNARDO L. (*See* Nava, et al.), 598
FORD, RALPH V. (*See* Rochelle and Ford), 463
FRASER, ROBERT S., AND ROSSALL, RICHARD E. Acute myocardial injury during cardiopulmonary bypass, 926
FRIMPTER, GEORGE W. (*See* Spritz, et al.), 715
FUJII, J. (*See* Okinaka, et al.), 319
FUJIOKA, TOSHYASU. (*See* Barbato, et al.), 340

G

GAMBOA, RAÚL. (*See* Peñaloza, et al.), 493
GARAMELLA, J. J. (*See* Caster, et al.), 658
GERBODE, FRANK. (*See* Baer, et al.), 652
GILBERT, LAWRENCE. (*See* Roseff, Levine, and Gilbert), 119
GILL, THOMAS J., III, MCBRIDE, RAYMOND A., AND DAMMIN, GUSTAVE J. Coronary embolism: report of three cases, 878
GOLDBERG, HARRY. (*See* Dickens and Goldberg), 8, 372
——. (*See* Sinha and Goldberg), 890
GROEBEN, J. VON DER. A comprehensive mapping of spatial vectorcardiographic data, 510
GROSSMAN, MILTON. Second degree heart block with Wenckebach phenomenon: its occurrence over a period of several years in a young healthy adult, 607
GUPTA, K. D. (*See* Sanghvi, et al.), 79
GUPTA, S. (*See* Padmavati, et al.), 112

H

HANSON, JOHN S. Complete right bundle branch block following cardiac surgery: report of two cases persisting after pulmonary valvulotomy and infundibulectomy, 275
HASHIBA, K. (*See* Okinaka, et al.), 319
HAUCK, ANNA J., ONGLEY, PATRICK A., AND NADAS, ALEXANDER S. The use of digoxin in infants and children, 443
HAYES, WILLIAM L. (*See* Dimond and Hayes), 929
HEJTMANCIK, MILTON R., HERRMANN, GEORGE R., AND WRIGHT, JAMES C. Paroxysmal supraventricular tachycardias complicating organic heart disease, 671

——. (*See* Zao, et al.), 65, 195, 920
HERRMANN, GEORGE R. (*See* Hejtmancik, Herrmann, and Wright), 671
——. (*See* Zao, et al.), 65, 195, 920
HIBBS, RICHARD G., BURCH, GEORGE E., AND PHILLIPS, JOHN H. The fine structure of the small blood vessels of normal human dermis and subcutis, 662
HOLLISTER, JAMES M., LUBASH, GLENN D., COHEN, BURTON D., BRAVEMAN, WARREN S., RUBIN, ALBERT L., AND LUCKEY, E. HUGH. Refractory edema treated with calcium chloride in combination with mercurial diuretics, 629
HUMERFELT, S., MÜLLER, O., AND STORSTEIN, O. The circulation in hyperthyroidism: a cardiac catheterization study before and after treatment, 87
HURST, J. WILLIS, AND BLACKARD, EMBREE. (Editorial) Inspection and palpation of pulsations on the front of the chest, 159
HUSNI, ELIAS. (*See* Sancetta, et al.), 212

I

IKEDA, M. (*See* Okinaka, et al.), 319
INMON, T. W. (*See* Cupp, et al.), 695
ISHIMI, Z. (*See* Okinaka, et al.), 319
ISOBE, TAKEHIKO. (*See* Toyoshima, et al.), 165

J

JACKSON, W. B. The functional activity of the human conjunctival capillary bed in hypertensive and normotensive subjects, 222
JODY, ALEXANDER. (*See* Scherf, et al.), 236
JOHNSTON, FRANK R. (*See* Spencer, et al.), 722

K

KANEKO, J. (*See* Okinaka, et al.), 319
KARNI, H. High-frequency features in the vectorcardiogram, 98
KARNI, HAIM S. TsÊ loop in left ventricular hypertrophy, 518
KARPMAN, HAROLD L. A method for indirect pulse recording, and its use in the diagnosis of aortic stenosis, 799
KATO, HIROSHI. (*See* Toyoshima, et al.), 165
KAVANAGH-GRAY, D., AND DRAKE, E. H. Complications of left heart catheterizations using the right transthoracic approach, 143
KERNEN, JULES A. Corrected transposition of the great vessels of the heart, 583
KLIP, W. Difficulties in the measurement of pulse-wave velocity, 806
——. (*See* Feer, et al.), 642
KRAMER, JAMES. (*See* Sancetta, et al.), 212
KRUEGER, JAMES D. (*See* Dick, et al.), 396
——. (*See* McCawley, et al.), 405
KURAMOTO, K. (*See* Okinaka, et al.), 319
KUTSUNA, YOSHIO. (*See* Toyoshima, et al.), 165

L

LACONI, ANTONELLO. The dynamics of the left ventricular border in chronic constrictive pericarditis: an analytic roentgenkymographic study with remarks on the "flat top and V" electrokymographic pattern, 73
LANGE, HENRIK F., AND AARSETH, SVERRE. The influence of anticoagulant therapy on the occurrence of cardiac rupture and hemopericardium following heart infarction. II. A controlled study of a selected treated group based on 1,044 autopsies, 257
——. (*See* Aarseth and Lange), 250
LARKS, S. D., AND DASGUPTA, K. Fetal electrocardiography, with special reference to early pregnancy, 701
LEE, PHILIP R. (*See* Williams, et al.), 107
LEIGHT, LEONARD, AND DAVIS, LAWRENCE A. The relation of the aortic root to the ventricular septum in tetralogy of Fallot, 129
LEPESCHKIN, E. A simple indexing system for electrocardiograms, 776
LEVINE, BURTON. (*See* Roseff, Levine, and Gilbert), 119
LEVINE, SAMUEL A. (Editorial) Pitfalls in interpreting coronary artery statistics, 639
——. (*See* Riss and Levine), 814, 831
LIKOFF, WILLIAM. (*See* Sinha, et al.), 264
LINDE, LEONARD M. (*See* Schmutzer and Linde), 761
LOGUE, R. BRUCE. (*See* Crevasse and Logue), 898
LOZANO, ELENA. (*See* Nava, et al.), 598
LUBASH, GLENN D. (*See* Hollister, et al.), 629
LUCKEY, E. HUGH. (*See* Hollister, et al.), 629

M

MALT, RONALD A. Ballistocardiogram during paralysis with succinylcholine, 245
MANNING, G. W. (*See* Sears and Manning), 591
MARTICORENA, EMILIO. (*See* Peñaloza, et al.), 493
MASTER, ARTHUR M. Iproniazid (Marsilid) in angina pectoris, 570
MCBRIDE, RAYMOND A. (*See* Gill, et al.), 878
MCCAWLEY, ELTON L., DICK, H. LENOX H., KRUEGER, JAMES D., AND VOISS, DANIEL V. A correlation between the therapeutic effectiveness of certain drugs in atrial fibrillation and their action on myocardial conduction, 405
——. (*See* Dick, et al.), 396
MCDEVITT, ELLEN. (*See* Escudero and McDevitt), 846
MELROSE, DENIS G. (*See* Baer, et al.), 652
MEREDITH, JESSE H. (*See* Spencer, Johnston, and Meredith), 722
MICHAELIDES, GEORGE. (*See* Aravanis, et al.), 126
MISRA, S. N. (*See* Sanghvi, et al.), 79
MOORE, CHARLES B. (*See* Birchall, et al.), 616
MÜLLER, O. (*See* Humerfelt, et al.), 87
MURATA, K. (*See* Okinaka, et al.), 319

N

NADAS, ALEXANDER S. (*See* Hauck, et al.), 443
NAGAYA, TERUO. (*See* Toyoshima, et al.), 165
NAIDU, R. (*See* Caster, et al.), 658
NAVA, ARMANDO, COMESAÑA, FRANCISCO, LOZANO, ELENA, FISHLEDER, BERNARDO L., AND SODI-PALLARES, DEMETRIO. With the technical assistance of Cuéllar, Adela. The effect of nicotinic acid, phenyl-ethyl-acetamide, and a combination of both drugs on hypercholesterolemic dogs and human beings, 598
NIITANI, H. (*See* Okinaka, et al.), 319
NORDYKE, ROBERT A., AND PEARCE, MORTON LEE. With the technical assistance of Yamashita, Joe. Renal adaptations to postural changes in chronic congestive heart failure, 202
NORMAN, ALAN. (*See* Baer, et al.), 652

O

OKINAKA, S., IKEDA, M., HASHIBA, K., MURATA, K., KANEKO, J., OZAWA, T., NIITANI, H., ISHIMI, Z., FUJII, J., TAKEDA, Y., KURAMOTO, K., TSUJI, M., AND TERASAWA, F. Studies on the control of coronary circulation. Part I. The effect of the stimulation of the nerves on the coronary circulation. Part II. The humoral effect on the coronary circulation, 319
ONGLEY, PATRICK A. (*See* Hauck, et al.), 443
OSBORN, JOHN J. (*See* Baer, et al.), 652
OZAWA, T. (*See* Okinaka, et al.), 319

P

PADMAVATI, S., GUPTA, S., AND PANTULU, G. V. A. Dietary fat, serum cholesterol levels, and incidence of atherosclerosis and hypertension in Delhi, India, 112
PANTULU, G. V. A. (*See* Padmavati, et al.), 112
PEARCE, MORTON LEE. (*See* Nordyke and Pearce), 202
PEÑALOZA, DANTE, ECHEVARRÍA, MAX, MARTICORENA, EMILIO, AND GAMBOA, RAÚL. Early electrocardiographic changes produced by ascending to high altitudes, 493
PERKINS, HERBERT A. (*See* Baer, et al.), 652
PHILLIPS, JOHN H. (*See* Hibbs, Burch, and Phillips), 662
PHILLIPS, R. W. The electrocardiogram in cor pulmonale secondary to pulmonary emphysema: A study of 18 cases proved by autopsy, 352
PILEGGI, FULVIO. (*See* Barbato, et al.), 340
PINTO LIMA, F. X., SPIRITUS, OSWALDO, AND TRANCHESI, JOÃO. Arrhythmias and vector electrocardiographic analysis of complete bundle branch block in Chagas' disease: A study of 103 autopsied cases, 501
PIPBERGER, HUBERT V. (*See* Ball and Pipberger), 611
PORTILLO, B. (*See* Espino-Vela, et al.), 856
PRIEST, EDWARD M. (*See* Caldwell and Priest), 737

R

RISS, EGON, AND LEVINE, SAMUEL A. Some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty. Part I, 814
——, and ——. Some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty. Part II, 831
ROCHELLE, DON, AND FORD, RALPH V. Evaluation of antihypertensive effects of S.9-390 (2-(oh-chlorobenzyl) imidazoline hydrochloride), 463
ROSEFF, IRWIN, LEVINE, BURTON, AND GILBERT, LAWRENCE. Lipothymoma simulating cardiomegaly: case report, 119
ROSENBERG, S. Z., BRAUN, K., AND STERN, S. Arterial pressure pulse contour and Valsalva maneuver in suspected aortic stenosis, 486
ROSSALL, RICHARD E. (*See* Fraser and Rossall), 926
ROWELL, N. R., AND STILL, W. J. S. Isolated dextrocardia associated with Lutembacher's syndrome, 60
RUBIN, ALBERT L. (*See* Hollister, et al.), 629
——. (*See* Spritz, et al.), 715
RUBIN, IRA L. (*See* Anderson and Rubin), 299
RUBIO, V. (*See* Espino-Vela, et al.), 856
RUEGSEGGER, J. M. Pneumococcal endocarditis, 867
RUSK, HOWARD A. (*See* Williams, et al.), 107

S

SANCETTA, SALVATORE M., KRAMER, JAMES, AND HUSNI, ELIAS. With the technical assistance of Heckman, Gladys, Janouskovec, Hanna, and Haney, Helen. The effects of "dry" heat on the circulation of man. I. General hemodynamics, 212
SANGHVI, L. M., MISRA, S. N., BANNERJI, K., AND GUPTA, K. D. Electrocardiogram in chronic severe anemia, 79
SARUHASHI, YOSHIKO. (*See* Toyoshima, et al.), 165
SCHERF, DAVID, BLUMENFELD, SERGE, YILDIZ, MUHTAR, AND JODY, ALEXANDER. The effect on atrial impulse formation of a hypertonic solution of sodium chloride applied focally, 236
SCHMUTZER, KARL J., AND LINDE, LEONARD M. Situs inversus totalis associated with complex cardiovascular anomalies, 761
SCHRIRE, V. The racial incidence of heart disease at Groote Schuur Hospital, Cape Town. Part I. Coronary vascular disease, 280
——. The racial incidence of heart disease at Groote Schuur Hospital, Cape Town. Part II. Hypertension and valvular disease of the heart, 742
SCHULTZ, JEPPE. Coronary arteriovenous aneurysm: review of literature, 431
SEARS, G. A., AND MANNING, G. W. Routine electrocardiography: postprandial T-wave changes, 591

SHERMAN, FRANK E., STENGEL, WILLIAM F., AND BAUERSFELD, S. RICHARD. Congenital stenosis of pulmonary veins at their atrial junctions, 908
SILVA, PAULO DE PAULA E. (*See* Barbato, et al.), 340
SINHA, KAMTA, URICCHIO, JOSEPH F., AND LIKOFF, WILLIAM. A clinical evaluation of cross-polar plication (posteromedial annuloplasty) in the surgical treatment of rheumatic mitral regurgitation, 264
SINHA, KAMTA P., AND GOLDBERG, HARRY. Marfan's syndrome: a case with complete dissection of the aorta, 890
SODI-PALLARES, DEMETRIO. (*See* Nava, et al), 598
SPENCER, MERRILL P., JOHNSTON, FRANK R., AND MEREDITH, JESSE H. The origin and interpretation of murmurs in coarctation of the aorta, 722
SPIRITUS, OSWALDO. (*See* Pinto Lima, et al.), 501
SPRITZ, NORTON, COHEN, BURTON D., FRIMPTER, GEORGE W., AND RUBIN, ALBERT L. Electrocardiographic interrelationship of the pre-excitation (Wolff-Parkinson-White) syndrome and myocardial infarction, 715
STENGEL, WILLIAM F. (*See* Sherman, et al.), 908
STERN, S. (*See* Rosenberg, et al.), 486
STERN, THOMAS N. (*See* Copeland and Stern), 291
STILL, W. J. S. (*See* Rowell and Still), 60
STOCKER, HAROLD H., AND ENTERLINE, H. T. "Cardio-vocal syndrome": laryngeal paralysis in intrinsic heart disease, 51
STORSTEIN, O. (*See* Humerfelt, et al.), 87

T

TAKEDA, Y. (*See* Okinaka, et al.), 319
TELLER, WALTER M. Congenital mitral atresia, 304
TENNEY, S. M. Correlative observations on the electrocardiogram and morphology of the heart of the Florida manatee, 933
TERASAWA, F. (*See* Okinaka, et al.), 319
THOMPSON, ROBERT G. (*See* Beard and Thompson), 313
TORNER-SOLER, M., BALAGUER-VINTRÓ, I., AND CARRASCO-AZEMAR, J. Cardiac dextroposition: hypoplasia of the right pulmonary artery with right venous pulmonary drainage into the inferior vena cava, 425
TORRES, J. (*See* Angelakos, et al.), 458
TOYOSHIMA, HIDEO, KATO, HIROSHI, ISOBE, TAKEHIKO, KUTSUNA, YOSHIO, NAGAYA, TERUO, AND SARUHASHI, YOSHIKO. Electrocardiogram and vectorcardiogram reconstruction and its application to clinical diagnosis of myocardial infarction, 165
TRANCHESI, JOÃO. (*See* Pinto Lima, et al.), 501
TSUJI, M. (*See* Okinaka, et al.), 319

U

URICCHIO, JOSEPH F. (*See* Sinha, et al.), 264

V

VAANE, J. P. (*See* Burger and Vaane), 29
VELOSO, A. (*See* Caster, et al.), 658
VOISS, DANIEL V. (*See* Dick, et al.), 396
——. (*See* McCawley, et al.), 405

W

WAGNER, G. R. (*See* Barnett and Wagner), 412
WAKAI, COOLIDGE S., AND EDWARDS, JESSE E. Pathologic study of persistent common atrioventricular canal, 779
WHITE, PAUL D. (*See* Williams, et al.), 107
WILLIAMS, BRYAN, WHITE, PAUL D., LEE, PHILIP R., AND RUSK, HOWARD A. Cardiac rehabilitation: a survey of cardiologists' opinions, 107
WOOD, EARL H. (*See* Wright and Wood), 64
WOOLVIN, S. C. (*See* Cupp, et al.), 695
WRIGHT, J. LEO, AND WOOD, EARL H. The value of aortic and radial pressure pulses in the diagnosis of cardiovascular disorders, 64
WRIGHT, JAMES C. (*See* Hejtmancik, et al.), 671

Y

YILDIZ, MUHTAR. (*See* Scherf, et al.), 236

Z

ZAO, ZANG Z., HERRMANN, GEORGE R., AND HEJTMANCIK, MILTON R. A study of cardiac vectors in the frontal plane, 65
——, ——, and ——. A vector study of the delta wave in "nondelayed" conduction, 920
——, ——, and ——. Spatial vector electrocardiography: method and average normal vector of P, QRS, and T in space, 195

Subject Index

A

Adrenaline, some aspects of role of noradrenaline and, in circulation (Euler), 469
Age factor: over and under 50 years; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 838
Altitudes, high, early electrocardiographic changes produced by ascending to (Peñaloza, et al.), 493
Anaesthesia (British Medical Bulletin), Vol. 14, No. 1, 155 (B. Rev.)
Anemia, severe, chronic, electrocardiogram in (Sanghvi, et al.), 79
Aneurysm, arteriovenous, coronary (Schultz), 431
  of ascending aorta caused by congenital syphilis (Beard and Thompson), 313
Angina pectoris and other muscular pain due to ischemia, treatment of, with iproniazid and isoniazid (Cossio), 113
  iproniazid (Marsilid) in (Master), 570
Année cardiologique internationale, Tome V, 150 (B. Rev.)
Announcements, 157, 318, 638, 798
Anomalies, cardiovascular, complex, situs inversus totalis associated with (Schmutzer and Linde), 761
Anticoagulant therapy, influence of, on occurrence of cardiac rupture and hemopericardium following heart infarction. I. Study of 89 cases of hemopericardium (81 of them cardiac ruptures) (Aarseth and Lange), 250
    II. Controlled study of selected treated group based on 1,044 autopsies (Lange and Aarseth), 257
Anticoagulative therapy, different concept of prothrombin time control for (Caldwell and Priest), 737
Aorta, ascending, aneurysm of, caused by congenital syphilis (Beard and Thompson), 313
  case with complete dissection of; Marfan's syndrome (Sinha and Goldberg), 890
  origin and interpretation of murmurs in coarctation of (Spencer, et al.), 722
Aortic and radial pressure pulses, value of, in diagnosis of cardiovascular disorders (Wright and Wood), 64
  root, relation of, to ventricular septum in tetralogy of Fallot (Leight and Davis), 129
  stenosis, method for indirect pulse recording, and its use in diagnosis of (Karpman), 799
    suspected, arterial pressure pulse contour and Valsalva maneuver in (Rosenberg, et al.), 486
Arrhythmias and vector electrocardiographic analysis of complete bundle branch block in Chagas' disease: study of 103 autopsied cases (Pinto Lima, et al.), 501
Arrhythmias—Cont'd
  cardiac; available methods of therapy (Bellet), 480
    electrolyte alterations in (Bellet), 482
    improvement in cardiac function (Bellet), 483
    recent advances in treatment of (Bellet), 479
Arterial hypertension, classics in, 154 (B. Rev.)
  pressure pulse contour and Valsalva maneuver in suspected aortic stenosis (Rosenberg, et al.), 486
  renal, obstruction, unilateral, hypertension due to: preliminary observations on contribution of differential renal clearance studies (Birchall, et al.), 616
Arteries, renal, both, human hypertension due to thrombotic occlusion of: report of case "cured" by surgical removal of thrombus (Castillo and Barrera), 769
Arteriosclerosis, clinical aspects of, 154 (B. Rev.)
Arteriovenous aneurysm, coronary (Schultz), 431
Artery, coronary, descending, anterior, traumatic laceration of, treated by ligation without myocardial infarction: report of case with review of literature (Carleton and Boyd), 136
    statistics, pitfalls in interpreting (Levine), 639
  pulmonary, right, with right venous pulmonary drainage into inferior vena cava, hypoplasia of; cardiac dextroposition (Torner-Soler, et al.), 425
Ascending aorta, aneurysm of, caused by congenital syphilis (Beard and Thompson), 313
Atherosclerosis and hypertension, dietary fat, serum cholesterol levels, and, incidence of, in Delhi, India (Padmavati, et al.), 112
  with consideration of; mechanisms of hypertension, 149 (B. Rev.)
Atresia, mitral, congenital (Teller), 304
Atrial dissociation, electrocardiographic demonstration of (Dimond and Hayes), 929
  fibrillation, correlation between therapeutic effectiveness of certain drugs in, and their action on myocardial conduction of (McCawley, et al.), 405
    occurrence of rapid ventricular rate during, as paradoxical manifestation of digitalis intoxication (Bacaner), 685
  flutter and ventricular tachycardia, simultaneous (Anderson and Rubin), 299
  impulse formation, effect on, of hypertonic solution of sodium chloride applied focally (Scherf, et al.), 236
  junctions, congenital stenosis of pulmonary veins at (Sherman, et al.), 908
Atrioventricular canal: associated acquired conditions (Wakai and Edwards), 791

Atrioventricular canal—Cont'd
congenital defects and conditions (Wakai and Edwards), 788
common, persistent, pathologic study of (Wakai and Edwards), 776
findings in primary congenital malformation (Wakai and Edwards), 788
sex, survival, and causes of death (Wakai and Edwards), 792
Auricular and ventricular septal defects, combined: study of five cases with postmortem confirmation in three (Espino-Vela, et al.), 856
fibrillation; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 831
A-V conducting system, dissociation with interference between pacemakers located within (Castellanos, et al.), 562

B

Ballistocardiogram during paralysis with succinylcholine (Malt), 245
Ballistocardiographic findings on J wave (Bodrogi), 95
Block, heart, second degree, with Wenckebach phenomenon: its occurrence over period of several years in young healthy adult (Grossman), 607
Blood, movement of heart and, in animals, anatomical essay, 317 (B. Rev.)
vessels, small, of normal human dermis and subcutis, fine structure of (Hibbs, et al.), 662
Book reviews, 149, 317, 478, 637, 795
Brustorgane, Erkrankungen der (Band I); Lehrbuch der Roentgenologischen Differentialdiagnostik, 795 (B. Rev.)
Bundle branch block, complete, arrhythmias and vector electrocardiographic analysis of, in Chagas' disease: study of 103 autopsied cases (Pinto Lima, et al.), 501
left, complicated by left ventricular myocardial infarction, electrocardiographic and vectorcardiographic changes in (Toyoshima et al.), 182
right, endocardial lead in (Dickens and Goldberg), 372
following cardiac surgery: report of two cases persisting after pulmonary valvulotomy and infundibulectomy (Hanson), 275
right, complicated by left ventricular myocardial infarction, electrocardiographic and vectorcardiographic changes in (Toyoshima et al.), 177
Bypass, cardiopulmonary, acute myocardial injury during (Fraser and Rossall), 926

C

Calcium chloride in combination with mercurial diuretics, refractory edema treated with (Hollister, et al.), 629
Capillary bed, conjunctival, human, functional activity of, in hypertensive and normotensive subjects (Jackson), 222
Cardiac arrhythmias, recent advances in treatment of (Bellet), 479
catheterization study before and after treatment; circulation in hyperthyroidism (Humerfelt, et al.), 87
dextroposition: hypoplasia of right pulmonary artery with right venous pulmonary drainage into inferior vena cava (Torner-Soler, et al.), 425
output measurement by injection method without arterial sampling (Feer, et al.), 642
rehabilitation: survey of cardiologists opinions (Williams, et al.), 107
rupture and hemopericardium, influence of anticoagulant therapy on occurrence of, following heart infarction. I. Study of 89 cases of hemopericardium (81 of them cardiac ruptures) (Aarseth and Lange), 250
II. Controlled study of selected treated group based on 1,044 autopsies (Lange and Aarseth), 257
surgery, complete right bundle branch block following: report of two cases persisting after pulmonary valvulotomy and infundibulectomy (Hanson), 275
vectors in frontal plane, study of (Zao, et al.), 65
Cardiomegaly, lipothymoma simulating: case report (Roseff, et al.), 119
Cardiopulmonary bypass, acute, myocardial injury during (Fraser and Rossall), 926
Cardiovascular anomalies, complex, situs inversus totalis associated with (Schmutzer and Linde), 761
disorders, value of aortic and radial pressure pulses in diagnosis of (Wright and Wood), 64
"Cardio-vocal syndrome": laryngeal paralysis in intrinsic heart disease (Stocker and Enterline), 51
Catheterizations, left heart, using right transthoracic approach, complications of (Kavanagh-Gray and Drake), 143
Chagas' disease, arrhythmias and vector electrocardiographic analysis of complete bundle branch block in: study of 103 autopsied cases (Pinto Lima, et al.), 501
Chaotic heart due to metastatic synovioma (Cupp, et al.), 695
Chest, inspection and palpation of pulsations on front of (Hurst and Blackard), 159
Children, use of digoxin in infants and (Hauck, et al.), 443
Chirurgie cardiaque, hypothermie et, 637 (B. Rev.)
Cholesterol, effect of drugs (nicotinic acid and phenyl-ethyl-acetamide) on different fractions of (Nava et al.), 602
serum, levels, dietary fat, and incidence of atherosclerosis and hypertension in Delhi, India (Padmavati, et al.), 112
Circulation, coronary, studies on control of. Part I. Effect of stimulation of nerves on coronary circulation. Part II. Humoral effect on coronary circulation (Okinaka, et al.), 319

Circulation—Cont'd
extracorporeal, serum electrolyte observations following (Baer, et al.), 652
in hyperthyroidism: cardiac catheterization study before and after treatment (Humerfelt, et al.), 87
of man, effects of "dry" heat on. I. General hemodynamics (Sancetta, et al.), 212
some aspects of role of noradrenaline and adrenaline in (Euler), 469
Coarctation of aorta, origin and interpretation of murmurs in (Spencer, et al.), 722
Conducting system, A-V, dissociation with interference between pacemakers located within (Castellanos, et al.), 562
Conduction, myocardial, correlation between therapeutic effectiveness of certain drugs in atrial fibrillation and their action on (McCawley, et al.), 405
electrocardiographic evaluation studies on quinidine-induced changes of (Dick, et al.), 396
"nondelayed," vector study of delta wave in (Zao, et al.), 920
Congestive heart failure, chronic, renal adaptations to postural changes in (Nordyke and Pearce), 202
Conjunctival capillary bed, human, functional activity of, in hypertensive and normotensive subjects (Jackson), 222
Constrictive pericarditis, chronic, dynamics of left ventricular border in: analytic roentgenkymographic study with remarks on "flat top and V" electrokymographic pattern (Laconi), 73
Contour, arterial pressure pulse, and Valsalva maneuver in suspected aortic stenosis (Rosenberg, et al.), 486
Cor pulmonale secondary to pulmonary emphysema, electrocardiogram in: study of 18 cases proved by autopsy (Phillips), 352
Coronary arteriovenous aneurysm, 431
artery, descending, anterior, traumatic laceration of, treated by ligation without myocardial infarction: report of case with review of literature (Carleton and Boyd), 136
statistics, pitfalls in interpreting (Levine), 639
circulation, studies on control of. Part I. Effect of stimulation of nerves on coronary circulation. Part II. Humoral effect on coronary circulation (Okinaka, et al.), 319
embolism: report of three cases (Gill, et al.), 878
occlusion, acute, effect of, upon movement of Evans blue dye into different areas of pig heart muscle (Caster, et al.), 658
vascular disease (Part I); racial incidence of heart disease at Groote Schuur Hospital, Cape Town (Schrire), 280

D

Delta wave, vector study of, in "nondelayed" conduction (Zao, et al.), 920
Dermis and subcutis, human, normal, fine structure of small blood vessels of (Hibbs, et al.), 662
Dextrocardia, isolated, associated with Lutembacher's syndrome (Rowell and Still), 60
Digitalis intoxication, occurrence of rapid ventricular rate during atrial fibrillation as paradoxical manifestation of (Bacaner), 685
Digoxin, use of, in infants and children (Hauck, et al.), 443
Dissociation, atrial, electrocardiographic demonstration of (Dimond and Hayes), 929
with interference between pacemakers located within A-V conducting system (Castellanos, et al.), 562
Diuretics, mercurial, refractory edema treated with calcium chloride in combination with (Hollister, et al.), 629
Drugs, certain, correlation between therapeutic effectiveness of, in atrial fibrillation and their action on myocardial conduction (McCawley, et al.), 405
hypotensive, 151 (B. Rev.)
sympatheticomimetic, case report and description of response to; severe orthostatic hypotension (Barnett and Wagner), 412
"Dry" heat, effects of, on circulation of man. I. General hemodynamics (Sancetta, et al.), 212

E

ECG changes, method of vector analysis of; myocardial infarction in Wolff-Parkinson-White syndrome (Angle), 36
Edema, refractory, treated with calcium chloride in combination with mercurial diuretics (Hollister, et al.), 629
Editorial. Inspection and palpation of pulsations on front of chest (Hurst and Blackard), 159
Pitfalls in interpreting coronary artery statistics (Levine), 639
Recent advances in treatment of cardiac arrhythmias (Bellet), 479
Vectorcardiography (Duchosal), 1
Elastomyofibrosis, endocardial, (EEMF), myocarditis with (Fisher and Davis), 537
Electrocardiogram and morphology of heart of Florida manatee, correlative observations on (Tenney), 933
and vectorcardiogram reconstruction and its application to clinical diagnosis of myocardial infarction (Toyoshima, et al.), 165
endocardial and precordial correlation of (Dickens and Goldberg), 17
in chronic severe anemia (Sanghvi, et al.), 79
in cor pulmonale secondary to pulmonary emphysema: study of 18 cases proved by autopsy (Phillips), 352
in scleroderma: analysis of 60 cases and review of literature (Escudero and McDevitt), 846
ventricular, precordial and endocardial, correlation of (Dickens and Goldberg), 8

Electrocardiograms, method of vector analysis of (Angle), 36
precordial, some observations concerning "nondipolar" fraction of; electrocardiographic cancellation (Brody and Copeland), 381
simple indexing system for (Lepeschkin), 776
some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 836
Electrocardiographic cancellation: some observations concerning "nondipolar" fraction of precordial electrocardiograms (Brody and Copeland), 381
changes, early, produced by ascending to high altitudes (Peñaloza, et al.), 493
demonstration of atrial dissociation (Dimond and Hayes), 929
evaluation studies on quinidine-induced changes of myocardial conduction (Dick, et al.), 396
interrelationship of pre-excitation (Wolff-Parkinson-White) syndrome and myocardial infarction (Spritz, et al), 715
vector, analysis, arrhythmias and, of complete bundle branch block in Chagas' disease: study of 103 autopsied cases (Pinto Lima, et al.), 501
Electrocardiography, clinical—interpretation on physiologic basis, 156 (B. Rev.)
fetal, with special reference to early pregnancy (Larks and Dasgupta), 701
routine: postprandial T-wave changes (Sears and Manning), 591
spatial vector: method and average normal vector of P, QRS, and T in space (Zao, et al.), 195
Electrokymographic pattern, "flat top and V," analytic roentgenkymographic study with remarks on; dynamics of left ventricular border in chronic constrictive pericarditis (Laconi), 73
Electrolyte, serum, observations following extracorporeal circulation (Baer, et al.), 652
Emboli; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 834
Embolism, coronary: report of three cases (Gill, et al.), 878
Emphysema, pulmonary, electrocardiogram in cor pulmonale secondary to: study of 18 cases proved by autopsy (Phillips), 352
Endocardial elastomyofibrosis (EEMF), myocarditis with (Fisher and Davis), 537
lead in complete right bundle branch block (Dickens and Goldberg), 372
precordial and, ventricular electrocardiogram, correlation of (Dickens and Goldberg), 8
thickening, observations concerning pathogenesis of, in adult heart (Fisher and Davis), 553
Endocarditis, pneumococcal (Ruegsegger), 867
Epicardial leads, direct, study of sequence of ventricular activation and QRS complex of pathologic human heart, using (Barbato, et al.), 340
Epicardial leads—Cont'd
Evans blue dye, effect of acute coronary occlusion upon movement of, into different areas of pig heart muscle (Caster, et al.), 658

F

Failure, congestive; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 835
Fat, dietary, serum cholesterol levels, and incidence of atherosclerosis and hypertension in Delhi, India (Padmavati, et al.), 112
Fetal electrocardiography, with special reference to early pregnancy (Larks and Dasgupta), 701
Fibrillation, atrial, correlation between therapeutic effectiveness of certain drugs in, and their action on myocardial conduction (McCawley, et al.), 405
occurrence of rapid ventricular rate during, as paradoxical manifestation of digitalis intoxication (Bacaner), 685
"Flat top and V" electrokymographic pattern, analytic roentgenkymographic study with remarks on; dynamics of left ventricular border in chronic constrictive pericarditis (Laconi), 73
Florida manatee, correlative observations on electrocardiogram and morphology of heart of (Tenney), 933
Flutter, atrial, and ventricular tachycardia, simultaneous (Anderson and Rubin), 299
Frontal plane, study of cardiac vectors in (Zao, et al.), 65

G

Great vessels of heart, corrected transposition of (Kernen), 583

H

Heart, adult, observations concerning pathogenesis of endocardial thickening in (Fisher and Davis), 553
and blood, movement of, in animals, anatomical essay, 317 (B. Rev.)
block, second degree, with Wenckebach phenomenon: its occurrence over period of several years in young healthy adult (Grossman), 607
chaotic, due to metastatic synovioma (Cupp, et al.), 695
corrected transposition of great vessels of (Kernen), 583
disease, intrinsic, laryngeal paralysis in: "cardio-vocal syndrome" (Stocker and Enterline), 51
organic, paroxysmal supraventricular tachycardias complicating (Hejtmancik, et al.), 671
racial incidence of, at Groote Schuur Hospital, Cape Town. Part I. Coronary vascular disease (Schrire), 280

Heart—Cont'd
Part II. Hypertension and valvular disease of heart (Schrire), 742
dog, hypothermic, ouabain on (Angelakos, et al.), 458
failure, congestive, chronic, renal adaptations to postural changes in (Nordyke and Pearce), 202
human, pathologic, study of sequence of ventricular activation and QRS complex of, using direct epicardial leads (Barbato, et al.), 340
left, catheterizations using right transthoracic approach, complications of (Kavanagh-Gray and Drake), 143
of Florida manatee, correlative observations on electrocardiogram and morphology of (Tenney), 933
Heat, "dry," effects of, on circulation of man. I. General hemodynamics (Sancetta, et al.), 212
Hemopericardium, influence of anticoagulant therapy on occurrence of cardiac rupture and, following heart infarction. I. Study of 89 cases of hemopericardium (81 of them cardiac ruptures) (Aarseth and Lange), 250
II. Controlled study of selected treated group based on 1,044 autopsies (Lange and Aarseth), 257
Hemoptysis, attacks of pulmonary edema or; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 831
Herzens, Physiologie des, 796 (B. Rev.)
Herzleiden, Operable; Einfuhrung in Klinik, Diagnostik und Operations-moglichkeiten, 637 (B. Rev.)
Humoral effect on coronary circulation (Part II); studies on control of coronary circulation (Okinaka, et al.), 332
Hypercholesterolemic dogs and human beings, effect of nicotinic acid, phenyl-ethyl-acetamide, and combination of both drugs on (Nava, et al.), 598
Hypertension and valvular disease of heart (Part II); racial incidence of heart disease at Groote Schuur Hospital, Cape Town (Schrire), 742
arterial, classics in, 154 (B. Rev.)
dietary fat, serum cholesterol levels, and incidence of atherosclerosis and, in Delhi, India (Padmavati, et al.), 112
due to unilateral renal arterial obstruction: preliminary observations on contribution of differential renal clearance studies (Birchall, et al.), 616
human, due to thrombotic occlusion of both renal arteries: report of case "cured" by surgical removal of thrombus (Castillo and Barrera), 769
mechanisms of: with consideration of atherosclerosis, 149 (B. Rev.)
portal, 317 (B. Rev.)
Hypertensive and normotensive subjects, functional activity of human conjunctival capillary bed in (Jackson), 222
Hyperthyroidism, circulation in: cardiac catheterization study before and after treatment (Humerfelt, et al.), 87
Hypertrophy, ventricular, left, TsÊ loop in (Karni), 518
Hypoplasia of right pulmonary artery with right venous pulmonary drainage into inferior vena cava; cardiac dextroposition (Torner-Soler, et al.), 425
Hypotension, orthostatic, severe: case report and description of response to sympatheticomimetic drugs (Barnett and Wagner), 412
Hypotensive drugs, 151 (B. Rev.)
Hypothermia, induced, physiology of, 156 (B. Rev.)
Hypothermic dog heart, ouabain on (Angelakos, et al.), 458
Hypothermie et chirurgie cardiaque, 637 (B. Rev.)

I

Infants and children, use of digoxin in (Hauck, et al.), 443
Infarction, heart, influence of anticoagulant therapy on occurrence of cardiac rupture and hemopericardium following. I. Study of 89 cases of hemopericardium (81 of them cardiac ruptures) (Aarseth and Lange), 250
II. Controlled study of selected treated group based on 1,044 autopsies (Lange and Aarseth), 257
myocardial, electrocardiogram and vectorcardiogram reconstruction and its application to clinical diagnosis of (Toyoshima, et al.), 165
electrocardiographic interrelationship of pre-excitation (Wolff-Parkinson-White) syndrome and (Spritz, et al.), 715
in Wolff-Parkinson-White syndrome: method of vector analysis of ECG changes (Angle), 36
traumatic laceration of anterior descending coronary artery treated by ligation without: report of case with review of literature (Carleton and Boyd), 136
Infarctions, fresh, electrocardiographic changes in (Toyoshima, et al.), 174
myocardial, old, electrocardiographic changes in (Toyoshima, et al.), 170
vectorcardiographic changes in (Toyoshima, et al.), 176
Infundibulectomy, report of two cases persisting after pulmonary valvulotomy and; complete right bundle branch block following cardiac surgery (Hanson), 275
Injury, myocardial, acute, during cardiopulmonary bypass (Fraser and Rossall), 926
Iproniazid and isoniazid, treatment of angina pectoris and other muscular pain due to ischemia with (Cossio, et al.), 113
(Marsilid) in angina pectoris (Master), 570
Ischemia, treatment of angina pectoris and other muscular pain due to, with iproniazid and isoniazid (Cossio), 113

Isoniazid, treatment of angina pectoris and other muscular pain due to ischemia with iproniazid and (Cossio), 113

J

J wave, ballistocardiographic findings on (Bodrogi), 95

L

Laryngeal paralysis in intrinsic heart disease: "cardio-vocal syndrome" (Stocker and Enterline), 51
Lead, endocardial, in complete right bundle branch block (Dickens and Goldberg), 372
Leads, endocardial, correlation of, with clinical and physiologic data (Dickens and Goldberg), 20
epicardial, direct, study of sequence of ventricular activation and QRS complex of pathologic human heart, using (Barbato, et al.), 340
Ligation, traumatic laceration of anterior descending coronary artery treated by, without myocardial infarction: report of case with review of literature (Carleton and Boyd), 136
Lipothymoma simulating cardiomegaly: case report (Roseff, et al.), 119
Loop, TsÊ, in left ventricular hypertrophy (Karni), 518
Lutembacher's syndrome, isolated dextrocardia associated with (Rowell and Still), 60

M

Manatee, Florida, correlative observations on electrocardiogram and morphology of heart of (Tenney), 933
Marfan's syndrome: case with complete dissection of aorta (Sinha and Goldberg), 890
Mercurial diuretics, refractory edema treated with calcium chloride in combination with (Hollister, et al.), 629
Metastatic synovioma, chaotic heart due to (Cupp, et al.), 695
Mitral atresia, congenital (Teller), 304
regurgitation, rheumatic, clinical evaluation of cross-polar plication (posteromedial annuloplasty) in surgical treatment of (Sinha, et al.), 264
valvular disease, some clinical notes on patients with, who have had mitral valvuloplasty. Part I (Riss and Levine), 814
Part II (Riss and Levine), 831
Mucopolysaccharides, chemistry and biology of, 796 (B. Rev.)
Murmurs, origin and interpretation of, in coarctation of aorta (Spencer, et al.), 722
Muscle, pig heart, effect of acute coronary occlusion upon movement of Evans blue dye into different areas of (Caster, et al.), 658
Muscular pain, other, angina pectoris and, due to ischemia, treatment of, with iproniazid and isoniazid (Cossio), 113
Myocardial conduction, correlation between therapeutic effectiveness of certain drugs in atrial fibrillation and their action on (McCawley, et al.), 405
electrocardiographic evaluation studies on quinidine-induced changes of (Dick, et al.), 396
infarction, electrocardiogram and vectorcardiogram reconstruction and its application to clinical diagnosis of (Toyoshima, et al.), 165
electrocardiographic interrelationship of pre-excitation (Wolff-Parkinson-White) syndrome and (Spritz, et al.), 715
in Wolff-Parkinson-White syndrome: method of vector analysis of ECG changes (Angle), 36
supraventricular tachycardia associated with (Hejtmancik, et al.), 681
traumatic laceration of anterior descending coronary artery treated by ligation without: report of case with review of literature (Carleton and Boyd), 136
injury, acute, during cardiopulmonary bypass (Fraser and Rossall), 926
Myocarditis with endocardial elastomyofibrosis (EEMF) (Fisher and Davis), 537

N

Nerves, effect of stimulation of, on coronary circulation (Part I); studies on control of coronary circulation (Okinaka, et al.), 319
Neuzeitlichen Brustwand und Extremitäten—Ableitungen in Praxis, 478 (B. Rev.)
Nicotinic acid, phenyl-ethyl-acetamide, and combination of both drugs, effect of, on hypercholesterolemic dogs and human beings (Nava, et al.), 598
"Nondelayed" conduction, vector study of delta wave in (Zao, et al.), 920
Noradrenaline and adrenaline, some aspects of role of, in circulation (Euler), 469

O

Occlusion, coronary, acute, effect of, upon movement of Evans blue dye into different areas of pig heart muscle (Caster, et al.), 658
thrombotic, of both renal arteries, human hypertension due to: report of case "cured" by surgical removal of thrombus (Castillo and Barrera), 769
Orthogonal vectorcardiogram, normal spatial QRS-T angle of (Ball and Pipberger), 611
Orthostatic hypotension, severe: case report and description of response to sympatheticomimetic drugs (Barnett and Wagner), 412
Ouabain on hypothermic dog heart (Angelakos, et al.), 458
Output, cardiac, measurement by injection method without arterial sampling (Feer, et al.), 642

P

P, QRS, and T, average normal vector of, in space, method and; spatial vector electrocardiography (Zao, et al.), 195
Pacemakers located within A-V conducting system, dissociation with interference between (Castellanos, et al.), 562
Pain, muscular, other, angina pectoris and, due to ischemia, treatment of, with iproniazid and isoniazid (Cossio), 113
Paralysis, laryngeal, in intrinsic heart disease: "cardio-vocal syndrome" (Stocker and Enterline), 51
with succinylcholine, ballistocardiogram during (Malt), 245
Paroxysmal supraventricular tachycardias complicating organic heart disease (Hejtmancik, et al.), 671
Pericarditis, constrictive, chronic, dynamics of left ventricular border in: analytic roentgenkymographic study with remarks on "flat top and V" electrokymographic pattern (Laconi), 73
Pharmacologic principles of medical practice, 153 (B. Rev.)
Phenyl-ethyl-acetamide, nicotinic acid, and combination of both drugs, effect of, on hypercholesterolemic dogs and human beings (Nava, et al.), 598
Phonokardiographie, Atlas und Kurzgefasstes Lehrbuch der, 797 (B. Rev.)
Plane, frontal, study of cardiac vectors in (Zao, et al.), 65
Plication, cross-polar (posteromedial annuloplasty), clinical evaluation of, in surgical treatment of rheumatic mitral regurgitation (Sinha, et al.), 264
Pneumococcal endocarditis (Ruegsegger), 867
Postural changes, renal adaptations to, in chronic congestive heart failure (Nordyke and Pearce), 202
Precordial and endocardial ventricular electrocardiogram, correlation of (Dickens and Goldberg), 8
electrocardiograms, some observations concerning "nondipolar" fraction of; electrocardiographic cancellation (Brody and Copeland), 381
Pre-excitation (Wolff-Parkinson-White) syndrome and myocardial infarction, electrocardiographic interrelationship of (Spritz, et al.), 715
Pregnancy and puerperium, Wenckebach periods in (Copeland and Stern), 291
early, fetal electrocardiography, with special reference to (Larks and Dasgupta), 701
Pressure pulse, arterial, contour and Valsalva maneuver in suspected aortic stenosis (Rosenberg, et al.), 486
pulses, aortic and radial, value of, in diagnosis of cardiovascular disorders (Wright and Wood), 64
Prothrombin time control for anticoagulative therapy, different concept of (Caldwell and Priest), 737
Puerperium, Wenckebach periods in pregnancy and (Copeland and Stern), 291
Pulmonary artery, right, with right venous pulmonary drainage into inferior vena cava, hypoplasia of; cardiac dextroposition (Torner-Soler, et al.), 425
edema or hemoptysis, attacks of; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 832
emphysema, electrocardiogram in cor pulmonale secondary to: study of 18 cases proved by autopsy (Phillips), 352
veins, congenital stenosis of, at atrial junctions (Sherman, et al.), 908
Pulmonic stenosis, ejection sound in (Crevasse and Logue), 900
second sound (Crevasse and Logue), 903
valvular: auscultatory and phonocardiographic characteristics (Crevasse and Logue), 898
Pulsations, inspection and palpation of, on front of chest (Hurst and Blackard), 159
Pulse, pressure, arterial, contour and Valsalva maneuver in suspected aortic stenosis (Rosenberg, et al.), 486
recording, indirect, method for, and its use in diagnosis of aortic stenosis (Karpman), 799
Pulseless disease: report of case (Aravanis, et al.), 126
Pulses, pressure, aortic and radial, value of, in diagnosis of cardiovascular disorders (Wright and Wood), 64
Pulse-wave velocity, difficulties in measurement of (Klip), 806
extraneous tissue interference (Klip), 809
with instrument registration (Klip), 806

Q

QRS complex, study of sequence of ventricular activation and, of pathologic human heart, using direct epicardial leads (Barbato, et al.), 340
P, and T, average normal vector of, in space, method and; spatial vector electrocardiography (Zao, et al.), 195
QRS-T angle, spatial, normal, of orthogonal vectorcardiogram (Ball and Pipberger), 611
Quinidine-induced changes of myocardial conduction; electrocardiographic evaluation studies on (Dick, et al.), 396

R

Racial incidence of heart disease at Groote Schuur Hospital, Cape Town. Part I. Coronary vascular disease (Schrire), 280
Part II. Hypertension and valvular disease of heart (Schrire), 742
Radial, aortic and, pressure pulses, value of, in diagnosis of cardiovascular disorders (Wright and Wood), 64
Reconstruction, electrocardiogram and vectorcardiogram, and its application to clinical diagnosis of myocardial infarction (Toyoshima, et al.), 165

Regurgitation, mitral, rheumatic, clinical evaluation of cross-polar plication (posteromedial annuloplasty) in surgical treatment of (Sinha, et al.), 264
Rehabilitation, cardiac: survey of cardiologists opinions (Williams, et al.), 107
Renal adaptations to postural changes in chronic congestive heart failure (Nordyke and Pearce), 202
arterial obstruction, unilateral, hypertension due to: preliminary observations on contribution of differential renal clearance studies (Birchall, et al.), 616
arteries, both, human hypertension due to thrombotic occlusion of: report of case "cured" by surgical removal of thrombus (Castillo and Barrera), 769
function tests, differential, use and interpretation of (Birchall, et al.), 619
Rheumatic mitral regurgitation, clinical evaluation of cross-polar plication (posteromedial annuloplasty) in surgical treatment of (Sinha, et al.), 264
Roentgenologischen Differentialdiagnostik, Lehrbuch der. Band I. Erkrankungen der Brustorgane, 795 (B. Rev.)
Rupture, cardiac, and hemopericardium, influence of anticoagulant therapy on occurrence of, following heart infarction. I. Study of 89 cases of hemopericardium (81 of them cardiac ruptures) (Aarseth and Lange), 250
II. Controlled study of selected treated group based on 1,044 autopsies (Lange and Aarseth), 257

S

S.9-390 (2-(o-chlorobenzyl) imidazoline hydrochloride), evaluation of antihypertensive effects of (Rochelle and Ford), 463
Scleroderma, electrocardiogram in: analysis of 60 cases and review of literature (Escudero and McDevitt), 846
Septal defects, auricular and ventricular, combined: study of five cases with postmortem confirmation in three (Espino-Vela, et al.), 856
Serum cholesterol levels, dietary fat, and incidence of atherosclerosis and hypertension in Delhi, India (Padmavati, et al.), 112
electrolyte observations following extracorporeal circulation (Baer, et al.), 652
Situs inversus totalis associated with complex cardiovascular anomalies (Schmutzer and Linde), 761
Sodium chloride, effect on atrial impulse formation of hypertonic solution of, applied focally (Scherf, et al.), 236
Space, criterion characterizing orientation of vectorcardiogram in (Burger and Vaane), 29
Spatial QRS-T angle, normal, of orthogonal vectorcardiogram (Ball and Pipberger), 611
vector electrocardiography: method and average normal vector of P, QRS, and T in space (Zao, et al.), 195
Spatial—Cont'd
vectorcardiographic data, comprehensive mapping of (Groeben), 510
Stenosis, aortic, method for indirect pulse recording, and its use in diagnosis of (Karpman), 799
suspected, arterial pressure pulse contour and Valsalva maneuver in (Rosenberg, et al.), 486
congenital, of pulmonary veins at atrial junctions (Sherman, et al.), 908
pulmonic, valvular: auscultatory and phonocardiographic characteristics (Crevasse and Logue), 898
(valve size), preoperative degree of, and postoperative clinical results; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 839
Subcutis, fine structure of small blood vessels of normal human dermis and (Hibbs, et al.), 662
Succinylcholine, ballistocardiogram during paralysis with (Malt), 245
Supraventricular tachycardias, paroxysmal, complicating organic heart disease (Hejtmancik, et al.), 671
Surgery, cardiac, complete right bundle branch block following: report of two cases persisting after pulmonary valvulotomy and infundibulectomy (Hanson), 275
Surgical treatment of rheumatic mitral regurgitation, clinical evaluation of cross-polar plication (posteromedial annuloplasty) in (Sinha, et al.), 264
Synovioma, metastatic, chaotic heart due to (Cupp, et al.), 695
Syphilis, congenital, aneurysm of ascending aorta caused by (Beard and Thompson), 313

T

T, P, QRS and, average normal vector of, in space, method and; spatial vector electrocardiography (Zao, et al.), 195
Tachycardia, ventricular, atrial flutter and, simultaneous (Anderson and Rubin), 299
Tachycardias, supraventricular, paroxysmal, complicating organic heart disease (Hejtmancik, et al.), 671
Tetralogy of Fallot, relation of aortic root to ventricular septum in (Leight and Davis), 129
Thrombotic occlusion of both renal arteries, human hypertension due to: report of case "cured" by surgical removal of thrombus (Castillo and Barrera), 769
Thrombus, report of case "cured" by surgical removal of; human hypertension due to thrombotic occlusion of both renal arteries (Castillo and Barrera), 769
Transthoracic approach, right, complications of left heart catheterizations using (Kavanagh-Gray and Drake), 143
Traumatic laceration of anterior descending coronary artery treated by ligation without myocardial infarction: re-

Traumatic—Cont'd
port of case with review of literature (Carleton and Boyd), 136
TsÊ loop in left ventricular hypertrophy (Karni), 518
T-wave changes, postprandial; routine electrocardiography (Sears and Manning), 591

V

Valsalva maneuver, arterial pressure pulse contour and, in suspected aortic stenosis (Rosenberg, et al.), 486
Valvular disease, mitral, some clinical notes on patients with, who have had mitral valvuloplasty. Part I (Riss and Levine), 814
Part II (Riss and Levine), 831
of heart, hypertension and (Part II); racial incidence of heart disease at Groote Schuur Hospital, Cape Town (Schrire), 742
pulmonic stenosis: auscultatory and phonocardiographic characteristics (Crevasse and Logue), 898
Valvuloplasty, mitral, some clinical notes on patients with mitral valvular disease who have had. Part I (Riss and Levine), 814
Part II (Riss and Levine), 831
pulmonary, and infundibulectomy, report of two cases persisting after; complete right bundle branch block following cardiac surgery (Hanson), 275
Vascular disease, coronary (Part I); racial incidence of heart disease at Groote Schuur Hospital, Cape Town (Schrire), 280
Vector analysis of ECG changes, method of; myocardial infarction in Wolff-Parkinson-White syndrome (Angle), 36
average normal, of P, QRS, and T in space, method and; spatial vector electrocardiography (Zao, et al.), 195
electrocardiographic analysis, arrhythmias and, of complete bundle branch block in Chagas' disease: study of 103 autopsied cases (Pinto Lima, et al.), 501
study of delta wave in "nondelayed" conduction (Zao, et al.), 920
Vectorcardiogram, criterion characterizing orientation of, in space (Burger and Vaane), 29
electrocardiogram and, reconstruction and its application to clinical diagnosis of myocardial infarction (Toyoshima, et al.), 165
high-frequency features in (Karni), 98
orthogonal, normal spatial QRS-T angle of (Ball and Pipberger), 611
Vectorcardiographic, spatial, data, comprehensive mapping of (Groeben), 510
Vectorcardiography (Duchosal), 1
Vectors, cardiac, in frontal plane, study of (Zao, et al.), 65
Veins, pulmonary, congenital stenosis of, at atrial junctions (Sherman, et al.), 908
Velocity, pulse-wave, difficulties in measurement of (Klip), 806
Vena cava, inferior, hypoplasia of right pulmonary artery with right venous pulmonary drainage into; cardiac dextroposition (Torner-Soler, et al.), 425
Venous pulmonary drainage, right, into inferior vena cava, hypoplasia of right pulmonary artery with; cardiac dextroposition (Torner-Soler, et al.), 425
Ventricular activation and QRS complex, study of sequence of, of pathologic human heart, using direct epicardial leads (Barbato, et al.), 340
auricular and, septal defects, combined: study of five cases with postmortem confirmation in three (Espino-Vela, et al.), 856
border, left, dynamics of, in chronic constrictive pericarditis: analytic roentgenkymographic study with remarks on "flat top and V" electrokymographic pattern (Laconi), 73
electrocardiogram, precordial and endocardial, correlation of (Dickens and Goldberg), 8
hypertrophy, left, TsÊ loop in (Karni), 518
rate, rapid, occurrence of, during atrial fibrillation as paradoxical manifestation of digitalis intoxication (Bacaner), 685
septum, relation of aortic root to, in tetralogy of Fallot (Leight and Davis), 129
tachycardia, atrial flutter and, simultaneous (Anderson and Rubin), 299
Vessels, blood, small, of normal human dermis and subcutis, fine structure of (Hibbs, et al.), 662
great, of heart, corrected transposition of (Kernen), 583
Volume sanguin des poumons chez l'homme, 152 (B. Rev.)

W

Wave, delta, vector study of, in "nondelayed" conduction (Zao, et al.), 920
J, ballistocardiographic findings on (Bodrogi), 95
Wenckebach periods in pregnancy and puerperium (Copeland and Stern), 291
phenomenon, second degree heart block with: its occurrence over period of several years in young healthy adult (Grossman), 607
Wolff-Parkinson-White syndrome, myocardial infarction in: method of vector analysis of ECG changes (Angle), 36

X

X-ray; some clinical notes on patients with mitral valvular disease who have had mitral valvuloplasty (Riss and Levine), 837

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Vol. 56, No. 6
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contents on page 1

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AMERICAN HEART JOURNAL

contents

December, 1958

Page

A Method for Indirect Pulse Recording, and Its Use in the Diagnosis of Aortic Stenosis
Harold L. Karpman, M.D., Los Angeles, Calif. 799

Difficulties in the Measurement of Pulse-Wave Velocity
W. Klip, M.D., Ph. D., Utrecht, Netherlands 806

Some Clinical Notes on Patients With Mitral Valvular Disease Who Have Had Mitral Valvuloplasty. Part I
Egon Riss, M.D., and Samuel A. Levine, M.D., Boston, Mass. 814

Some Clinical Notes on Patients With Mitral Valvular Disease Who Have Had Mitral Valvuloplasty. Part II
Egon Riss, M.D., and Samuel A. Levine, M.D., Boston, Mass. 831

The Electrocardiogram in Scleroderma: Analysis of 60 Cases and Review of the Literature
Jorge Escudero, M.D., and Ellen McDevitt, M.D., New York, N.Y. 846

Combined Auricular and Ventricular Septal Defects: A Study of Five Cases With Postmortem Confirmation in Three
J. Espino-Vela, M.D., B. Portillo, M.D., V. Rubio, M.D., and S. Aranda, M.D., Mexico, D.F. 856

Pneumococcal Endocarditis
J. M. Ruegsegger, M.D., Pearl River, N.Y. 867

Coronary Embolism: Report of Three Cases
Thomas J. Gill, III, M.D., Raymond A. McBride, M.D., and Gustave J. Dammin, M.D., Boston, Mass. 878

contents

continued

AMERICAN HEART JOURNAL

Page

MARFAN'S SYNDROME: A CASE WITH COMPLETE DISSECTION OF THE AORTA
Kamta P. Sinha, M.D., and Harry Goldberg, M.D., Philadelphia, Pa. 890

VALVULAR PULMONIC STENOSIS: AUSCULTATORY AND PHONOCARDIOGRAPHIC CHARACTERISTICS
Lamar Crevasse, M.D., and R. Bruce Logue, M.D., Emory University, Ga. 898

CONGENITAL STENOSIS OF PULMONARY VEINS AT THEIR ATRIAL JUNCTIONS
Frank E. Sherman, M.D., William F. Stengel, M.D., and S. Richard Bauersfeld, M.D., Pittsburgh, Pa. 908

A VECTOR STUDY OF THE DELTA WAVE IN "NONDELAYED" CONDUCTION
Zang Z. Zao, M.D., George R. Herrmann, M.D., and Milton R. Hejtmancik, M.D., Galveston, Tex. 920

ACUTE MYOCARDIAL INJURY DURING CARDIOPULMONARY BYPASS
Robert S. Fraser, M.D., and Richard E. Rossall, M.D., Edmonton, Canada 926

AN ELECTROCARDIOGRAPHIC DEMONSTRATION OF ATRIAL DISSOCIATION
E. Grey Dimond, M.D., and William L. Hayes, M.D., Kansas City, Kans. 929

CORRELATIVE OBSERVATIONS ON THE ELECTROCARDIOGRAM AND MORPHOLOGY OF THE HEART OF THE FLORIDA MANATEE
S. M. Tenney, M.D., Hanover, N.H. 933

Index

INDEX 939

(Editorial and Business Communications on Page 4)

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*Ford, R.V., and Moyer, J.H.: Rauwolfia Toxicity in the Treatment of Hypertension, Postgrad. Med. *23*:41 (Jan.) 1958.

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1. Bellet, S., Finkelstein, D., and Gilmore, H.: A.M.A. Archives Internal Med. 100:750, 1957.

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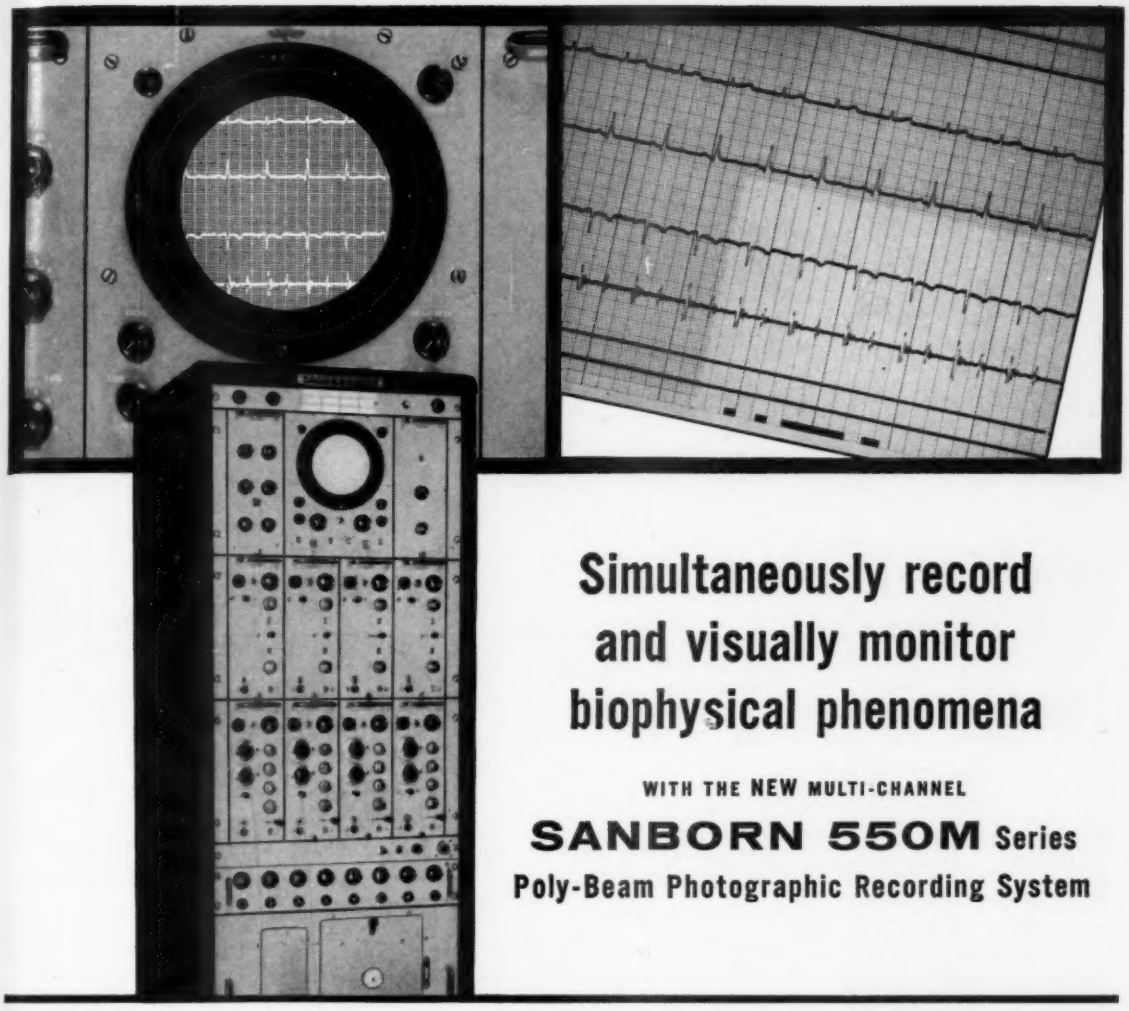

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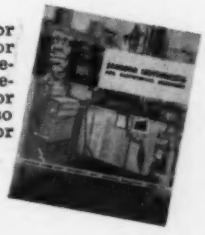

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Riseman, J. E. F., *et al.*: Circulation *17*:22, 1958

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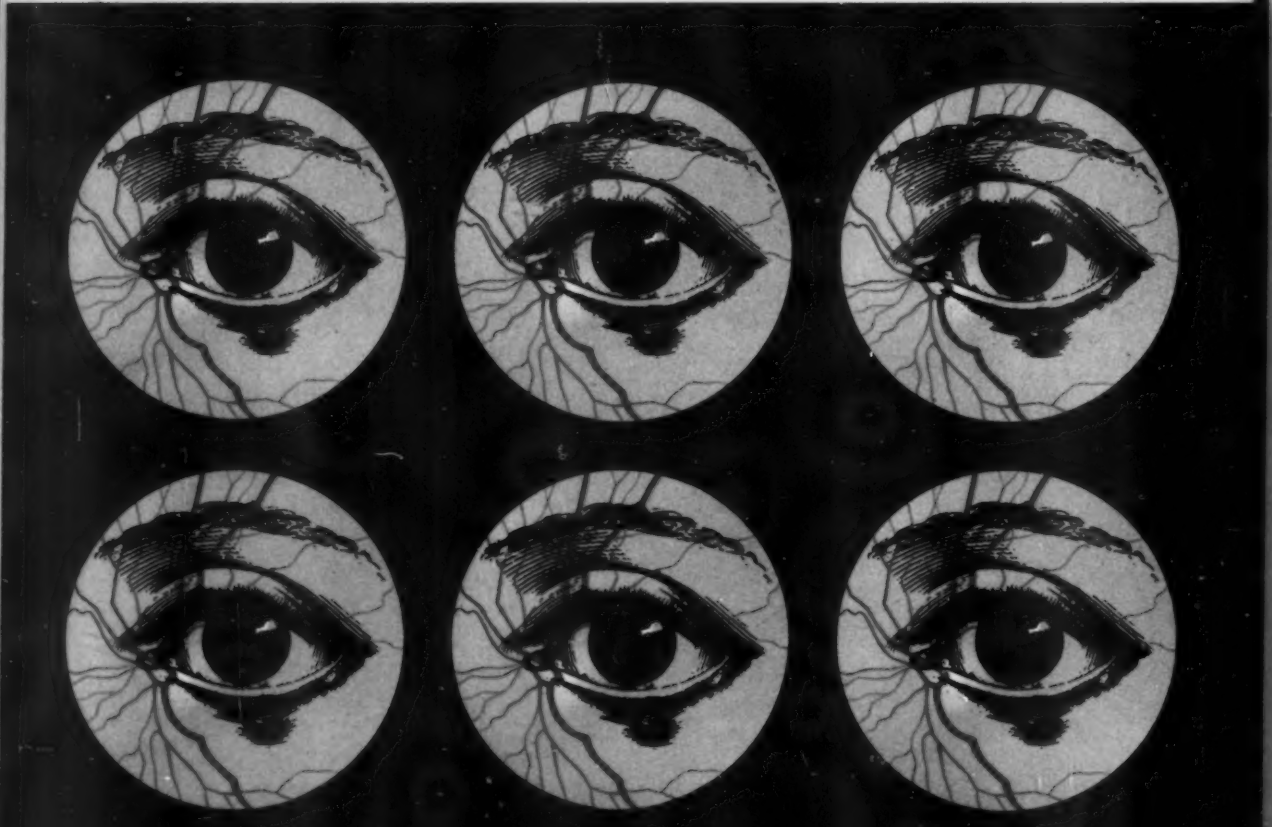

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the ideal
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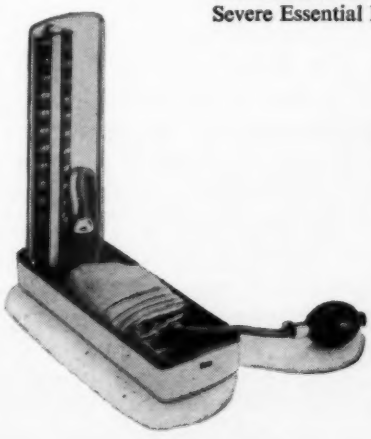
REFERENCES: 1. Cecil and Loeb: Textbook of Medicine, 9th Ed.; W. B. Saunders Co., Phila.; p. 1257. 2. Lindauer and Hafkenschiel: Hexamethonium Chloride with Reserpine in the Treatment of Severe Essential Hypertension; Angiology; 9:1 (Feb.,) 1958.



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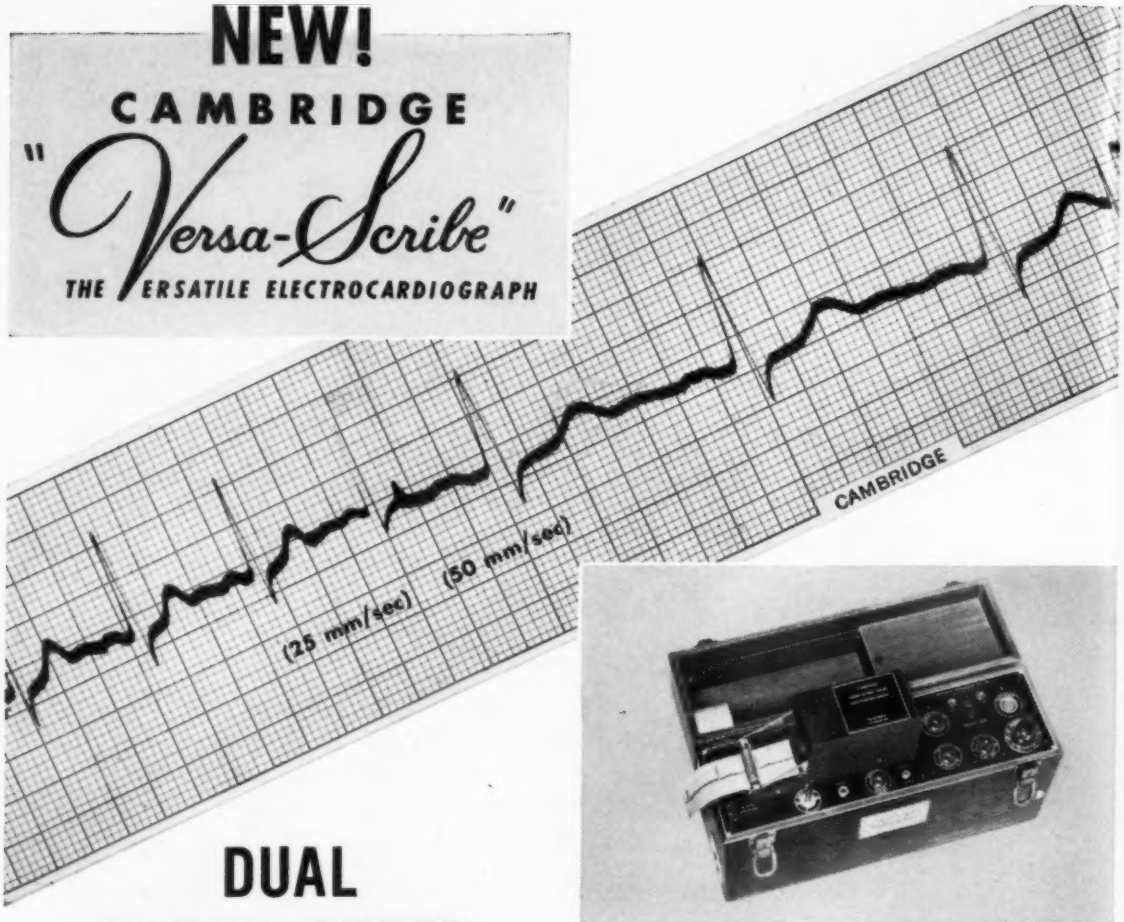

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Send for Bulletin 188 VS

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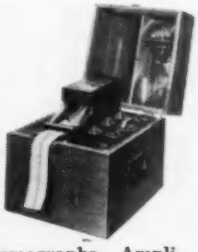

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1. Russek, H. I.: Postgrad. Med. *19*:562 (June) 1956. 2. Samuels, S. S.: Angiology *9*:245 (Aug.) 1958. 3. Burrell, Z. L., et al.: Am. J. Cardiol. *1*:624 (May) 1958. 4. Samuels, S. S.: Angiology, in press. 5. Ende, M.: To be published.

Bed of Digitalis purpurea
with Campanula (Canterbury Bells) in foreground

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and the psychic tension

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In angina pectoris

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secobarbituric acid ..... 50 mg.

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*Feinblatt, T.M. and Ferguson, E.A.: New Eng. J. of Med. (Feb. 21) 1957.

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FINNERTY, F. A., Buchholz, J. H. and Tuckman, J.: J.A.M.A. **166**:141, Jan. 11, 1958.

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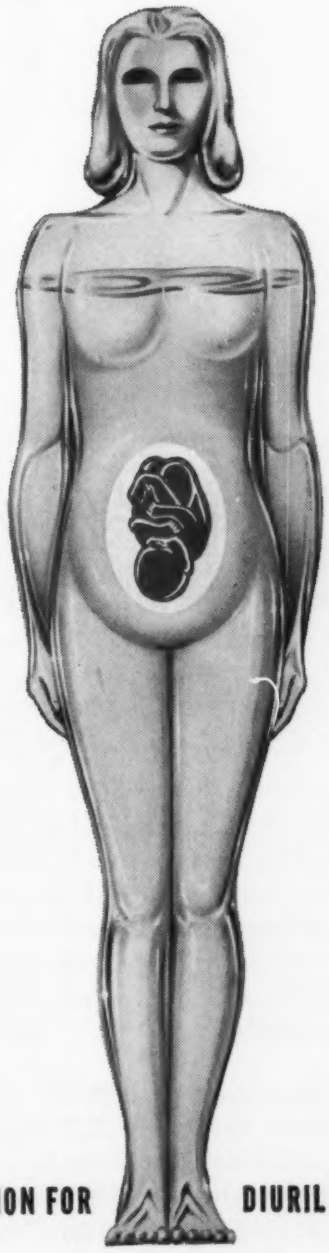

.....caused an excellent diuresis, with reduction of edema, weight, blood pressure, and albuminuria...."

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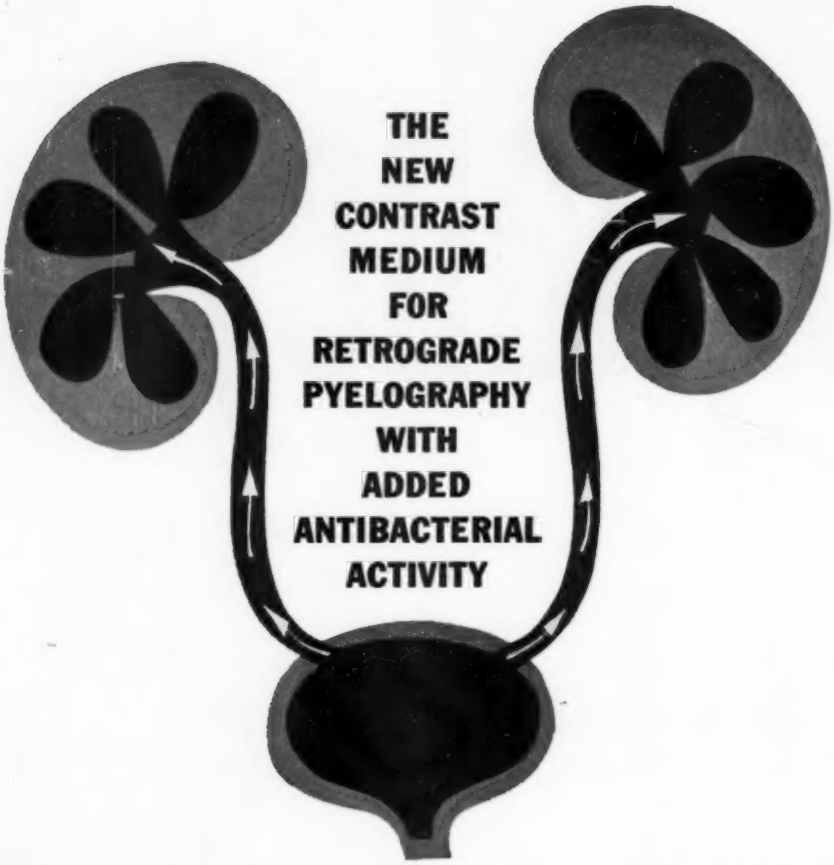

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for maximum opacification when urinary tract infection is present or suspected

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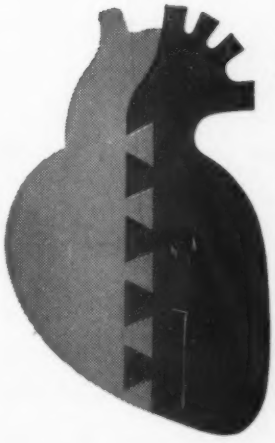
Squibb Quality—the Priceless Ingredient

'RETROGRAFIN' AND 'RENOGRAFIN'® ARE SQUIBB TRADEMARKS

PREVENT
both cause and fear of
ANGINA ATTACKS

proven safety for long-term use



Miltrate*

NEW DOVETAILED THERAPY COMBINES IN ONE TABLET

prolonged relief from anxiety and tension with **MILTOWN®** — The *original* meprobamate, discovered and introduced by Wallace Laboratories

\+

sustained coronary vasodilation with **PETN** — pentaerythritol tetranitrate a leading, long-acting nitrate

"In diagnosis and treatment [of cardiovascular diseases] . . . the physician must deal with both the emotional and physical components of the problem simultaneously."[1]

The addition of Miltown to PETN, as in Miltrate,"...appears to be more effective than [PETN] alone in the control of coronary insufficiency and angina pectoris."[2]

Miltrate is recommended *for prevention* of angina attacks, *not for relief* of acute attacks.

Supplied: Bottles of 50 tablets.

Each tablet contains: 200 mg. Miltown + 10 mg. pentaerythritol tetranitrate.

Usual dosage: 1 or 2 tablets q.i.d. *before meals* and at bedtime.

Dosage should be individualized. *For clinical supply and literature, write Dept. 23F*

1. *Friedlander, H. S.: The role of ataraxics in cardiology. Am. J. Card.* **1**:*395, March 1958.*
2. *Shapiro, S.: Observations on the use of meprobamate in cardiovascular disorders. Angiology* **8**:*504, Dec. 1957.*

WALLACE LABORATORIES, *New Brunswick, N. J.*

CML-7187 *TRADE-MARK

Why Oatmeal Merits Preference

The large number of breakfast cereals available may well give the erroneous impression that they are all more or less alike, and that the choice of one over the other is merely for the sake of variety.

Nothing could be further from the truth.

Oatmeal merits its position as a breakfast cereal widely recommended by physicians because it presents notable advantages.

First, oatmeal is known to provide more good quality protein than any other whole-grain cereal.

Next, oatmeal requires no fortification; it ranks highest among whole-grain cereals in thiamine and is significant in its content of other B vitamins and important minerals.

Just as important to the physician who prescribes a cereal food is oatmeal's inviting warmth, its delicious nut-like flavor, its ease of digestion, and the ready availability of its contained nutrients. Whether it be for an infant's first solid feeding...for the geriatric patient...for patients with gastrointestinal problems...and in many other situations, oatmeal makes a real contribution to the day's nutritional needs.

Quaker Oats and Mother's Oats, the two brands of oatmeal offered by The Quaker Oats Company, are identical. Both brands are available in the Quick (cooks in one minute) and the Old-Fashioned varieties which are of equal nutrient value.

The Quaker Oats Company
CHICAGO

i
a

in angina pectoris... "safety helmet" against effort-emotion precipitants

Pentraline*

PENTRALINE shields your patient against both the effort and the emotion that can precipitate an angina attack.

The PETN shields him against the effects of *effort*. Safe, long acting and well tolerated, this coronary vasodilator improves the blood flow through the coronary arteries.

The harmful effects of *emotion* are combatted by the other two components of PENTRALINE. Reliable sedative action comes from BUTISOL SODIUM®; and a mild, safe, tranquilizing effect is provided by small doses of reserpine.

Each scored pink tablet contains: Pentaerythritol tetranitrate—10 mg.; BUTISOL SODIUM® butabarbital sodium—10 mg.; Reserpine—0.05 mg.

Dosage: The usual dose is one tablet four times a day administered *before* meals and at bedtime.

Note: PENTRALINE is not intended for treatment of acute attacks of angina pectoris, but rather for routine daily use as a preventive measure.

*Trade-mark

198A53

McNEIL

McNeil Laboratories, Inc.
Philadelphia 32, Pa.

In hypotensive crises . . .

a powerful aid to increase myocardial efficiency

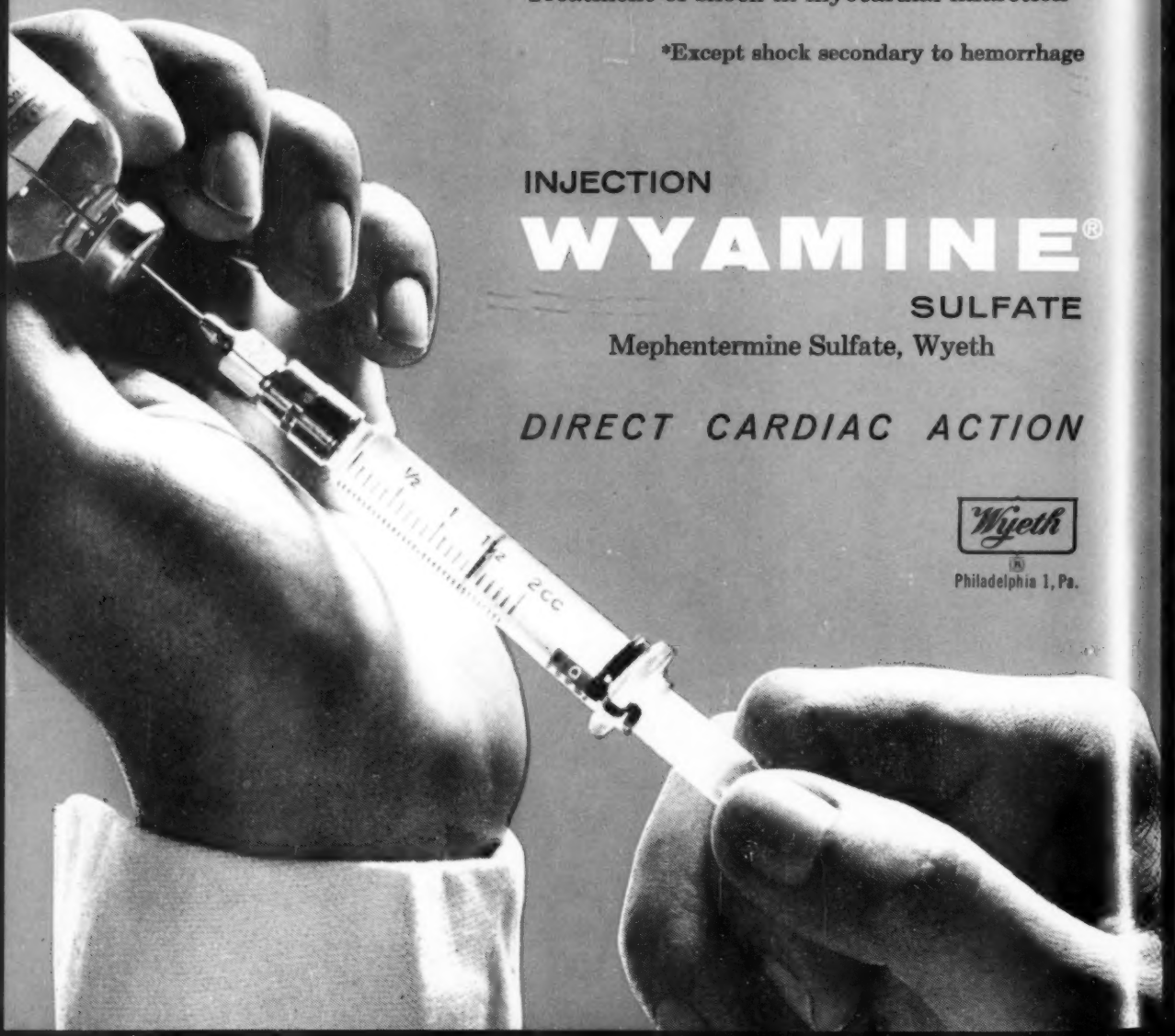
In acute hypotensive states,* WYAMINE exerts a positive inotropic effect by increasing the force of contraction of the myocardium. Simultaneously, it increases the rate of conduction and shortens the refractory period of the heart.

Indicated in:

Prevention and treatment of hypotension resulting from anesthesia or surgical procedures

Treatment of shock in myocardial infarction

*Except shock secondary to hemorrhage



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SULFATE

Mephentermine Sulfate, Wyeth

DIRECT CARDIAC ACTION

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VITAMIN K_1

the only available preparation chemically identical with naturally-occurring vitamin K_1 ... "has a more prompt, more potent and more prolonged effect than the vitamin K analogues"[2]

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1. Wright, I. S.: Early use of anticoagulants in treatment of myocardial infarction, J.A.M.A. 163: 918-921, March 16, 1957.
2. Council on Pharmacy and Chemistry: New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Co., 1956, p. 505.

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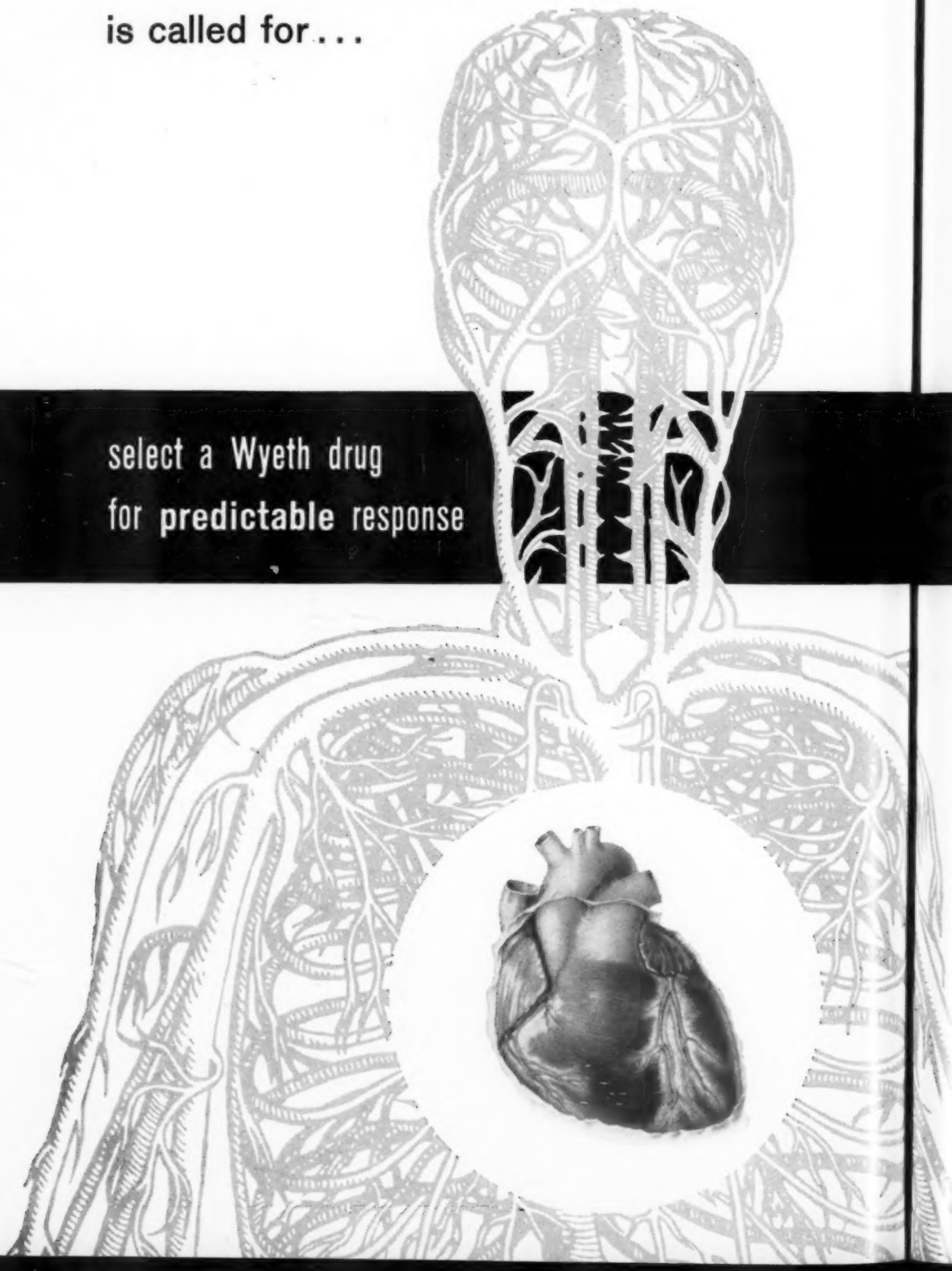
is called for . . .

select a Wyeth drug
for **predictable** response



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Indicated as adjunctive therapy to relieve psychic stress often associated with cardiovascular disorders. EQUANIL relieves tension, mental and muscular, and produces the desired calmness.

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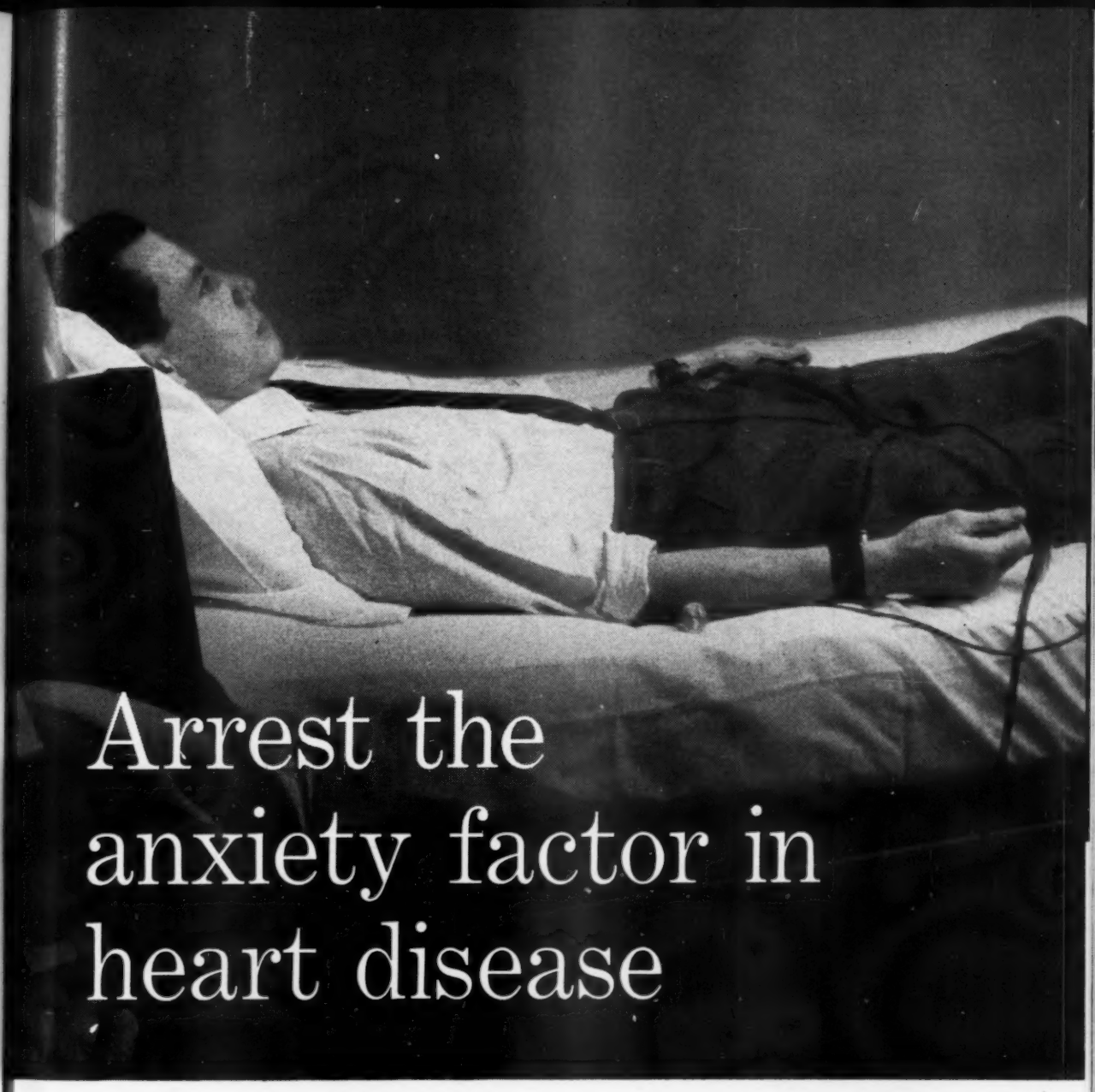

Arrest the anxiety factor in heart disease

without affecting autonomic function

"A cardiac breakdown might be forestalled or arrested" by effective treatment of nervous tension and anxiety.* ■ Adjunctive therapy with meprobamate "definitely reduced nervous tension and anxiety" in all heart patients (80 cases), and enhanced recovery from acute cardiac episodes in many cases.*

**Waldman, S. and Pelner, L.: Management of anxiety associated with heart disease. Am. Pract. & Digest Treat. 8:1075, July 1957.*

Because of its unexcelled safety, *Miltown is well suited for tranquilization of chronic heart patients. It is well tolerated, relatively nontoxic, and produces no blood dyscrasias, liver impairment, parkinsonism, or nasal stuffiness. It does not mask toxicity of other drugs.*

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Miltown is the original *meprobamate, discovered and introduced by* WALLACE LABORATORIES *New Brunswick, N. J.*

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SUPPLIED:

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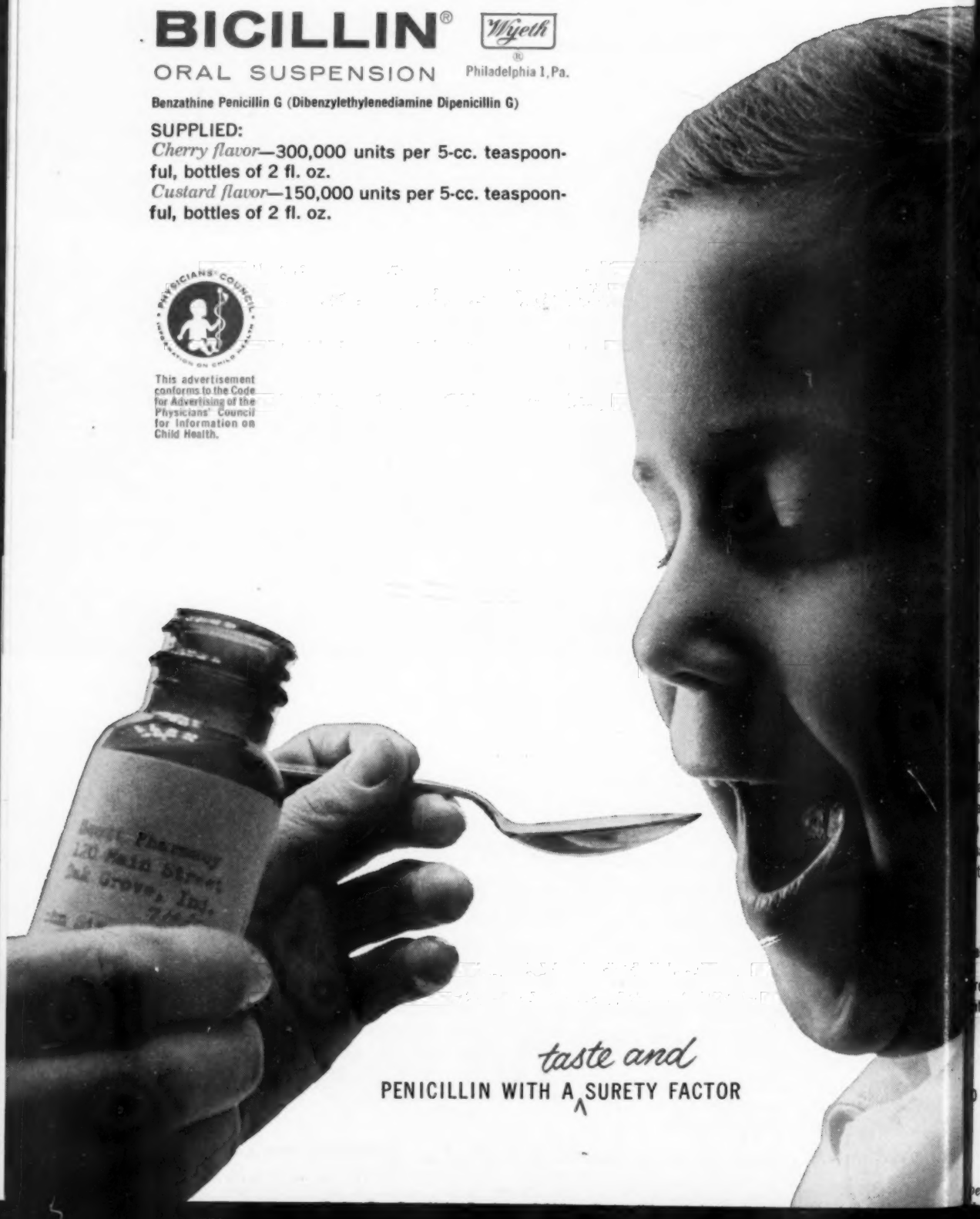

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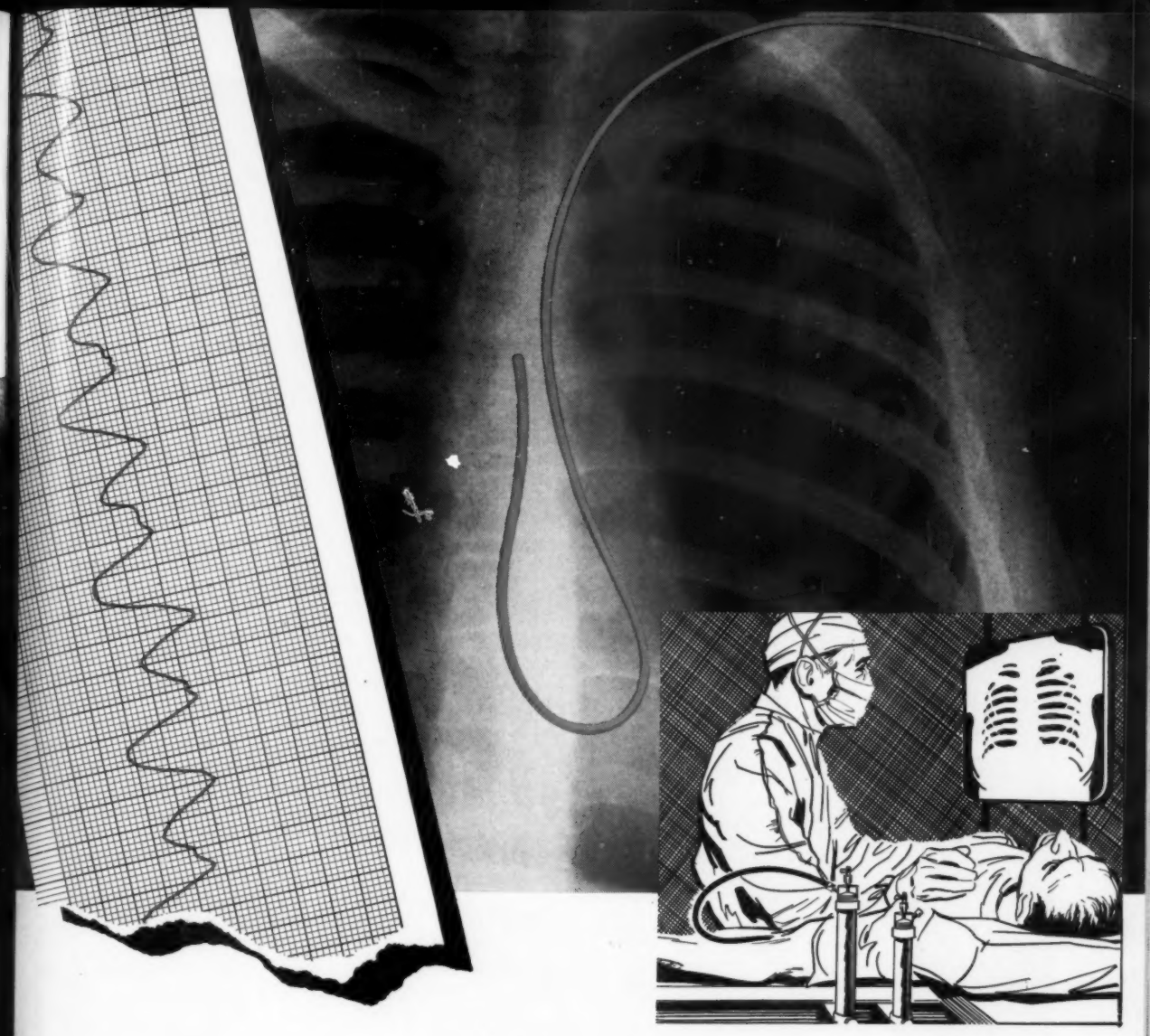

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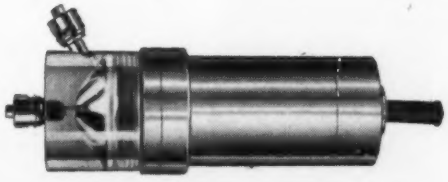

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"If one digitalis agent were to be recommended for its adaptability to the many and varied clinical contingencies, we believe Digoxin would be the drug of choice."

Lown, B., and Levine, S. A.: Current Concepts in Digitalis Therapy, Boston, Little, Brown & Company, 1954, p. 23, par. 2.

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0.25 mg. scored (white) 0.5 mg. scored (green)	0.5 mg. in 2 cc. (I.M. or I.V.)	0.05 mg. in 1 cc.

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As an adjunct to appropriate specific treatment, EQUANIL gives rapid, essential control of the psychic tensions that intensify and complicate cardiac and cardiovascular symptoms. "On control of the emotional complications [with EQUANIL in 41 varied patients], treatment in every case was less intensive and prolonged than ordinarily would have been expected."[1]

1. Friedlander, H.S.: Am. J. Cardiol. *1*:395 (March) 1958.

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Meprobamate

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Relieves tension—mental and muscular

IT IS SO REWARDING AND SO EASY TO SWITCH TO "WIDE SAFETY MARGIN"

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REWARDING BECAUSE—Gitaligin provides safe, smooth, controlled cardiac therapy.

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DIGITOXIN	0.1 MG.	0.5 MG.
DIGOXIN	0.5 MG.	0.5 MG.

SUPPLIED—Gitaligin TABLETS 0.5 mg., bottles of 30 and 100.
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*BIBLIOGRAPHY AVAILABLE ON REQUEST.

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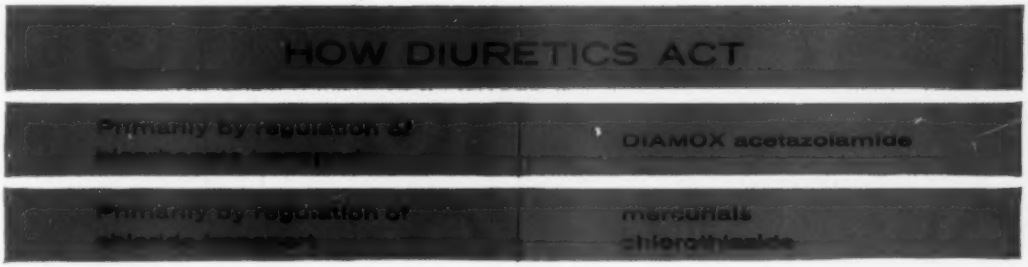
DIAMOX*

bicarbonate-regulating diuretic

Acetazolamide Lederle



1 Advantages of DIAMOX in single-drug diuresis

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DIAMOX is virtually nontoxic . . . has not caused renal or gastric irritation . . . has no pronounced effect on blood pressure. It is rapidly excreted, does not accumulate in the body, permits convenient dosage adjustment, allows unbroken sleep. Small, tasteless, easy-to-take tablets . . . usual dosage, only one a day.

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2 Advantages of DIAMOX in intensive, two-drug diuresis

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Except for the title there is very little similarity between this enlarged and expanded edition of "PRACTICE OF MEDICINE" and the five previous editions. Where the first five editions were almost entirely the work of Doctor Meakins, he has served only as Editor-in-Chief of this edition. Working under him were 24 Associate Editors—and they, in turn, had 87 contributors do most of the actual writing. As a result the book is entirely new and different.

Designed to assist the practitioner of medicine in solving the numerous puzzles and problems which he daily encounters, this book is arranged according to diseases of the various systems and organs—a plan that lends itself to simplicity. It is eminently a clinical book with symptoms being given particular prominence. The pathological basis of symptoms is everywhere stressed, and the bedside recognition and interpretation of clinical signs is described with a sustained interest and lucidity rarely found in tomes of this size.

The major responsibility of this revision was placed in the hands of the 24 Associate Editors—each unto his own particular realm; each with a broad understanding of the unity of medicine as a whole; each realizing that the wide subject of man's disabilities could not be viewed as made of segregated entities, but that there must be coordination of the anatomic, physiologic, emotional, and environmental whole.

In each section where applicable, reference to the so-called psychosomatic patterns and psychologic aspects has been made, and there is, finally, a section on Psychosomatic Medicine, designed to knit the general concepts of this branch into an integrated whole.

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When anxiety and tension complicate **HIGH BLOOD PRESSURE**

Miltown

Miltown in addition to ganglionic blocking therapy resulted in subjective and objective improvement in 35 of 37 patients. On the antihypertensive agent alone, only 28 patients improved.[1]

1. Nussbaum, H. E., Leff, W. A., Mattia, V. D., Jr. and Hillman, E.: An effective combination in the treatment of the hypertensive patient. Am. J. M. Sc. **234**: 150, Aug. 1957.

Literature and samples on request

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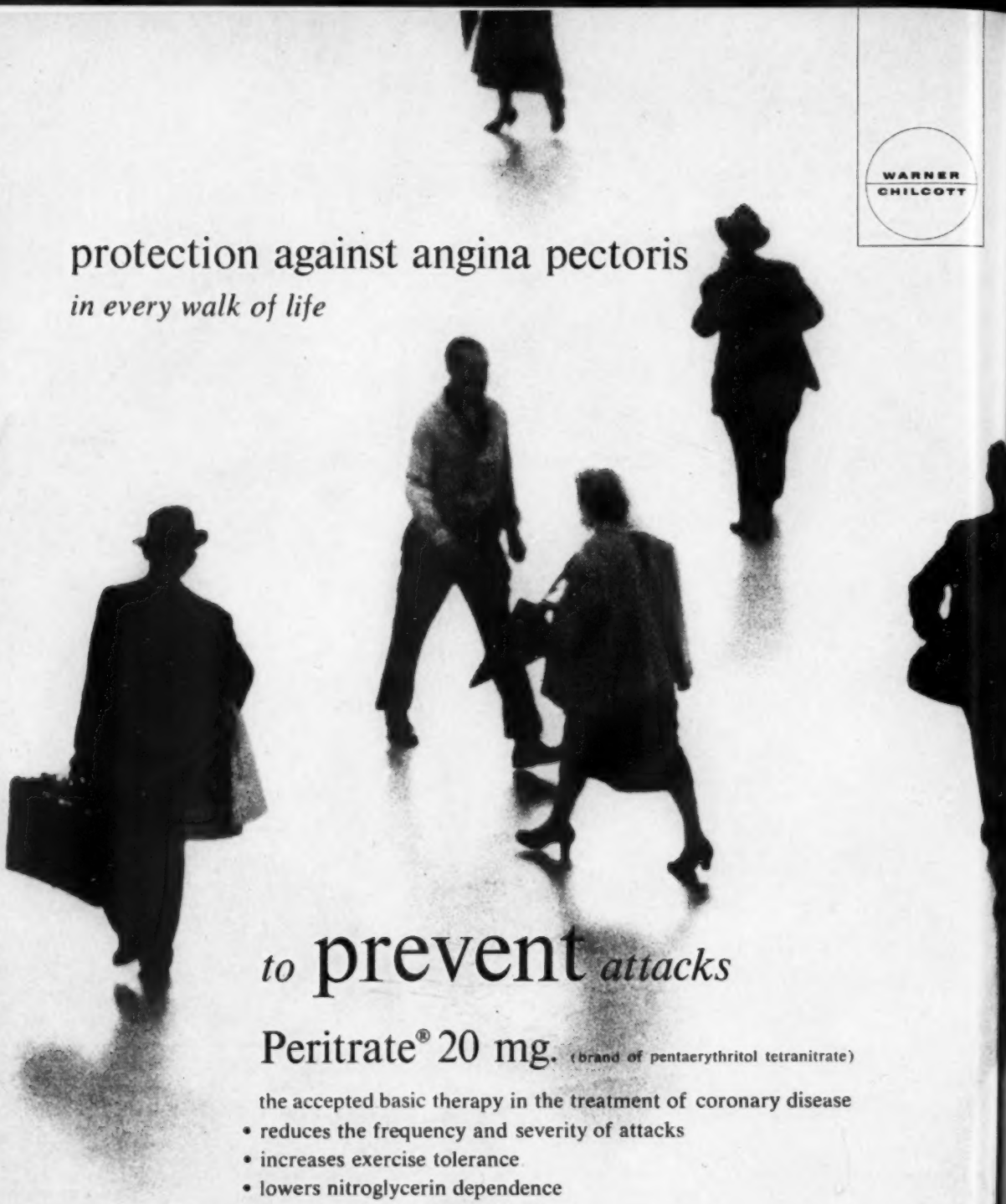
CHILCOTT

protection against angina pectoris
in every walk of life



to prevent *attacks*

Peritrate® 20 mg. (brand of pentaerythritol tetranitrate)

the accepted basic therapy in the treatment of coronary disease

- reduces the frequency and severity of attacks
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- lowers nitroglycerin dependence
- improves abnormal EKG findings

to relieve the acute *attack*

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Peritrate with Nitroglycerin

replaces ordinary nitroglycerin in the patient taking Peritrate (not meant to replace Peritrate)

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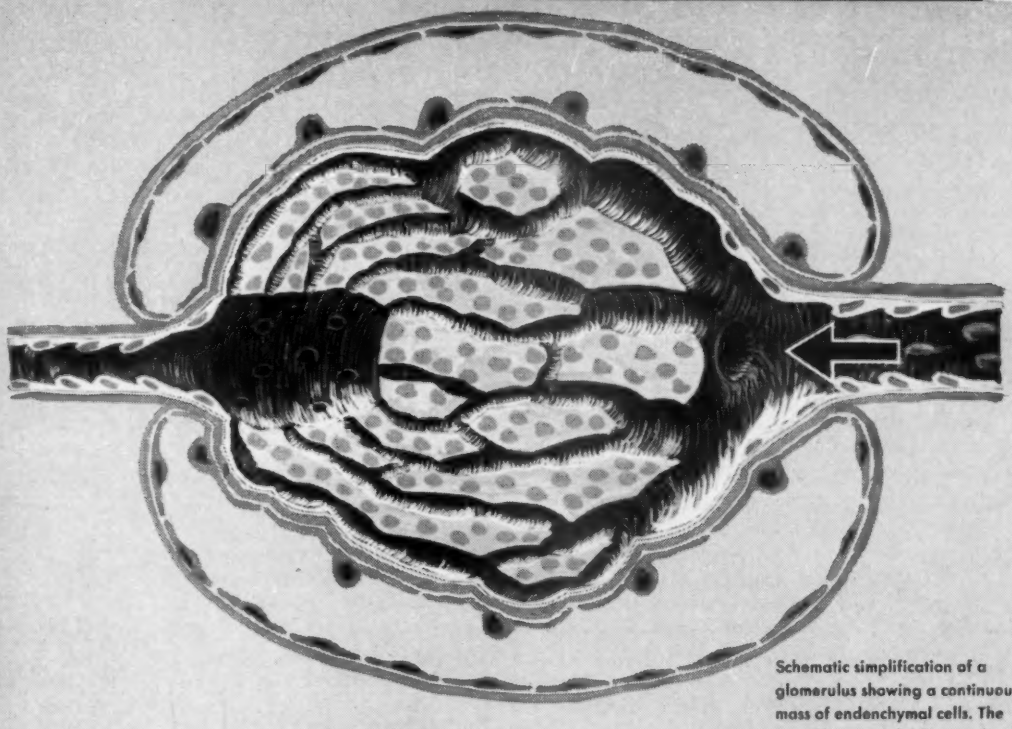

Schematic simplification of a glomerulus showing a continuous mass of endenchymal cells. The vas afferens (right) forms a large chamber from which arise channels in which blood streams through the endenchymal mass. The channels branch and become narrower distally and frequently anastomose. Several branches converge so that a limited number of terminal trunks enter the vas efferens (left). The endothelial cells of the vasa afferens and efferens often project, droplike, into the lumen.

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BRAND OF AMISOMETRADINE

MAINTAINS AN EDEMA-FREE STATE WITHOUT FASTNESS OR TOXICITY

The experience of 358 practicing physicians with more than 2,000 edematous patients indicates that Rolicton produces favorable results in a majority of patients. Excellent control of edema may be observed even in patients not responding to or intolerant to other diuretics.

A recent report by Settel* is typical. Thirty-six patients had taken various mercurial or non-mercurial oral diuretics for two years prior to Rolicton therapy. Because of intolerance to the preparations or owing to their ineffectiveness, "most . . . had ceased to take these drugs or had been taking them only sporadically." The results of Rolicton therapy were "highly satisfactory" and tolerance "was excellent." Most welcome to the patients was the reduction in the necessity for parenteral mercurials.

Rolicton promptly causes removal of edema fluid and on a small dosage patients are maintained in a "dry" state for long periods of time. This oral, non-mercurial, non-sulfonamide diuretic "appears to be the drug of choice* in the treatment of long-standing edema."

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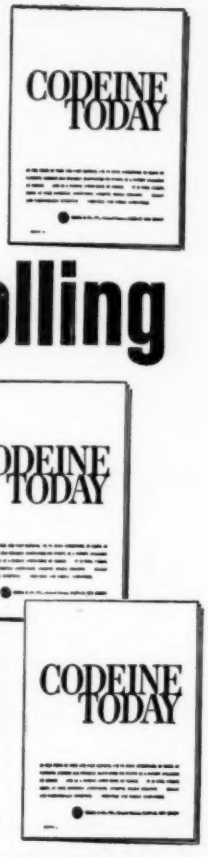

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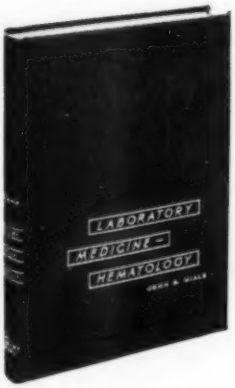

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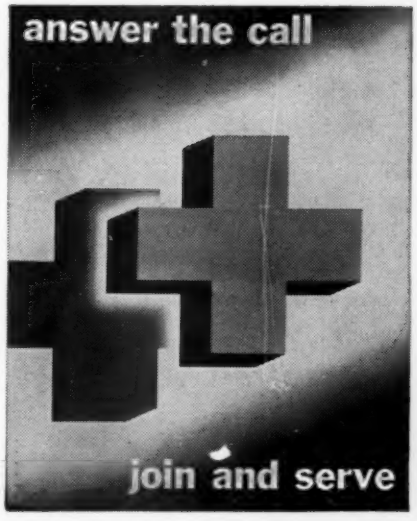

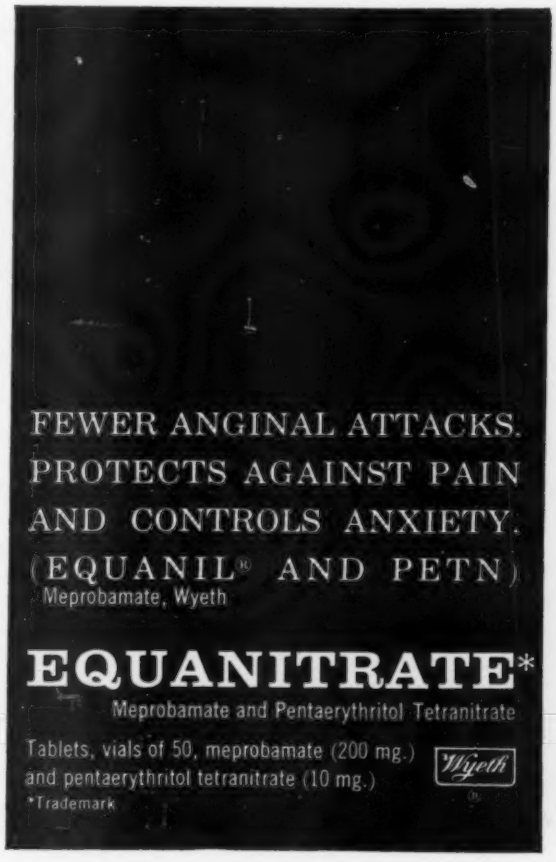

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Christmas Seals	44
Ciba Pharmaceutical Products (Singoserp)	17, 45
Davies, Rose & Company, Ltd. (Digitalis)	14
Jones & Hauck Box Corps., Jesse (Volume File)	43
Lederle Laboratories, a Division of American Cyanamid Company (Diamox)	35
Leeming & Company, Inc., Thos. (Metamine)	5
Lilly and Company, Eli (Crystodigin)	Fourth Cover
NcNeil Laboratories, Inc. (Pentraline)	23
March of Dimes, The	46
Merck & Company, Inc. (Codeine)	41
Merck Sharp & Dohme, Div. of Merck & Co., Inc. (Diuril)	18, 19
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National Dairy Council (Fats)	10
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Quaker Oats Company, The (Oatmeal)	22
Riker Laboratories (Rauwiloid)	3
Roerig Company, J. B. (Cartrax)	13
Sanborn Company (Poly-Beam Photographic Recording System)	7
Searle & Company, G. D. (Rolicton)	39
Squibb & Sons, E. R. (Raudixin)	Second Cover
Squibb & Sons, E. R. (Retrografin)	20
Statham Instruments, Inc. (Manometers)	31
Walker Laboratories (Hedulin)	48
Wallace Laboratories (Miltrate)	21
Wallace Laboratories (Miltown)	29
Wallace Laboratories (Miltown)	37
Warner-Chilcott (Methium)	11
Warner-Chilcott (Peritrate)	38
White Laboratories, Inc. (Gitaligin)	34
Wyeth Laboratories (Bicillin Injection)	9
Wyeth Laboratories (Equalysen)	15
Wyeth Laboratories (Wyamine)	24
Wyeth Laboratories (Ans Lysen, Equanil, Purodigin, Thiomerin, Wyamine)	26, 27
Wyeth Laboratories (Bicillin Oral)	30
Wyeth Laboratories (Equanil)	33
Wyeth Laboratories (Equanitrate)	41, 43, 47
Wynn Pharmacal Corporation (Quinaglute)	6

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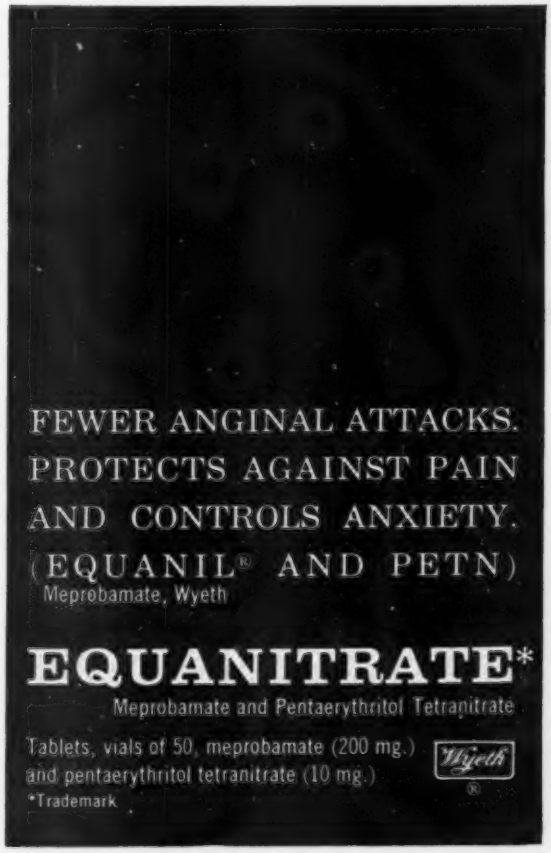

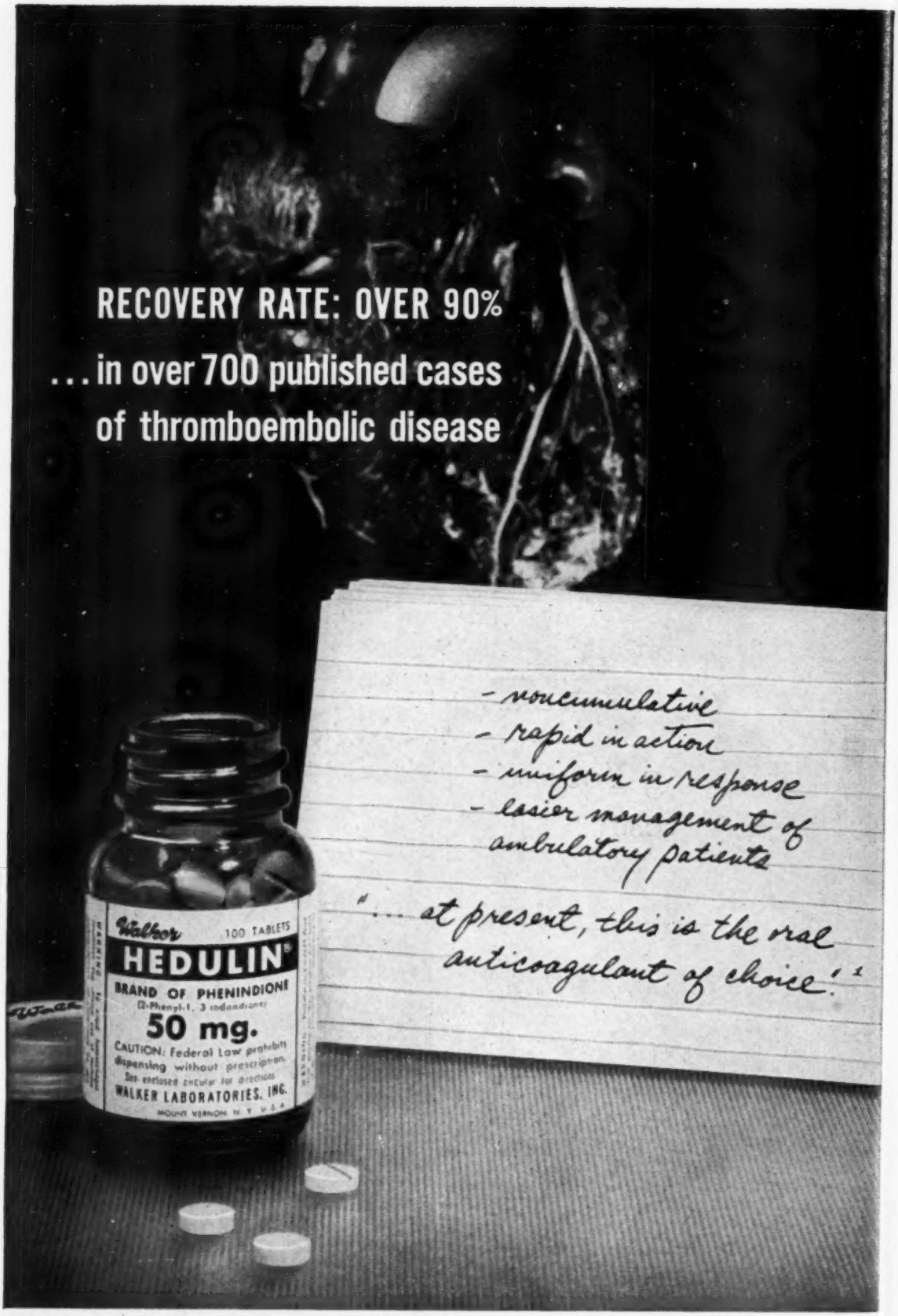
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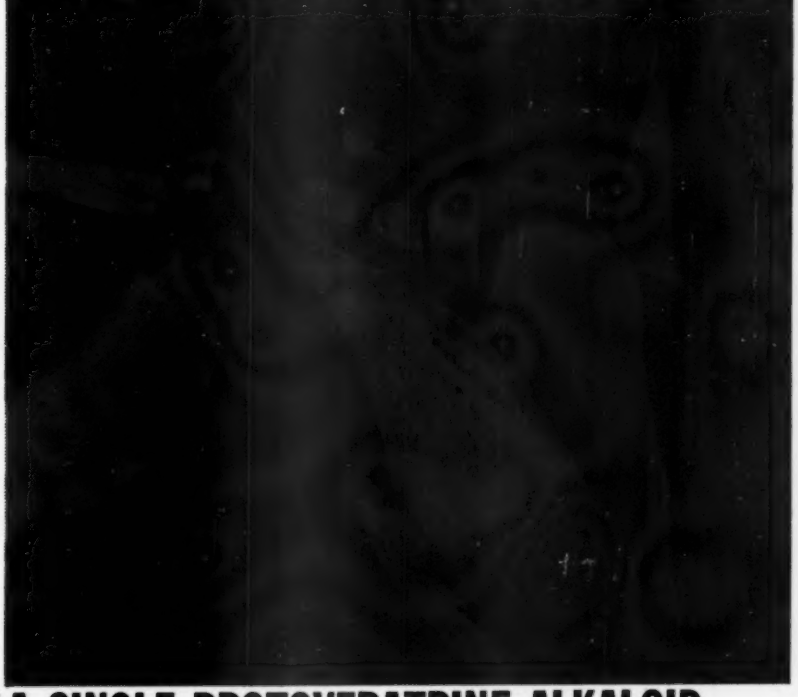

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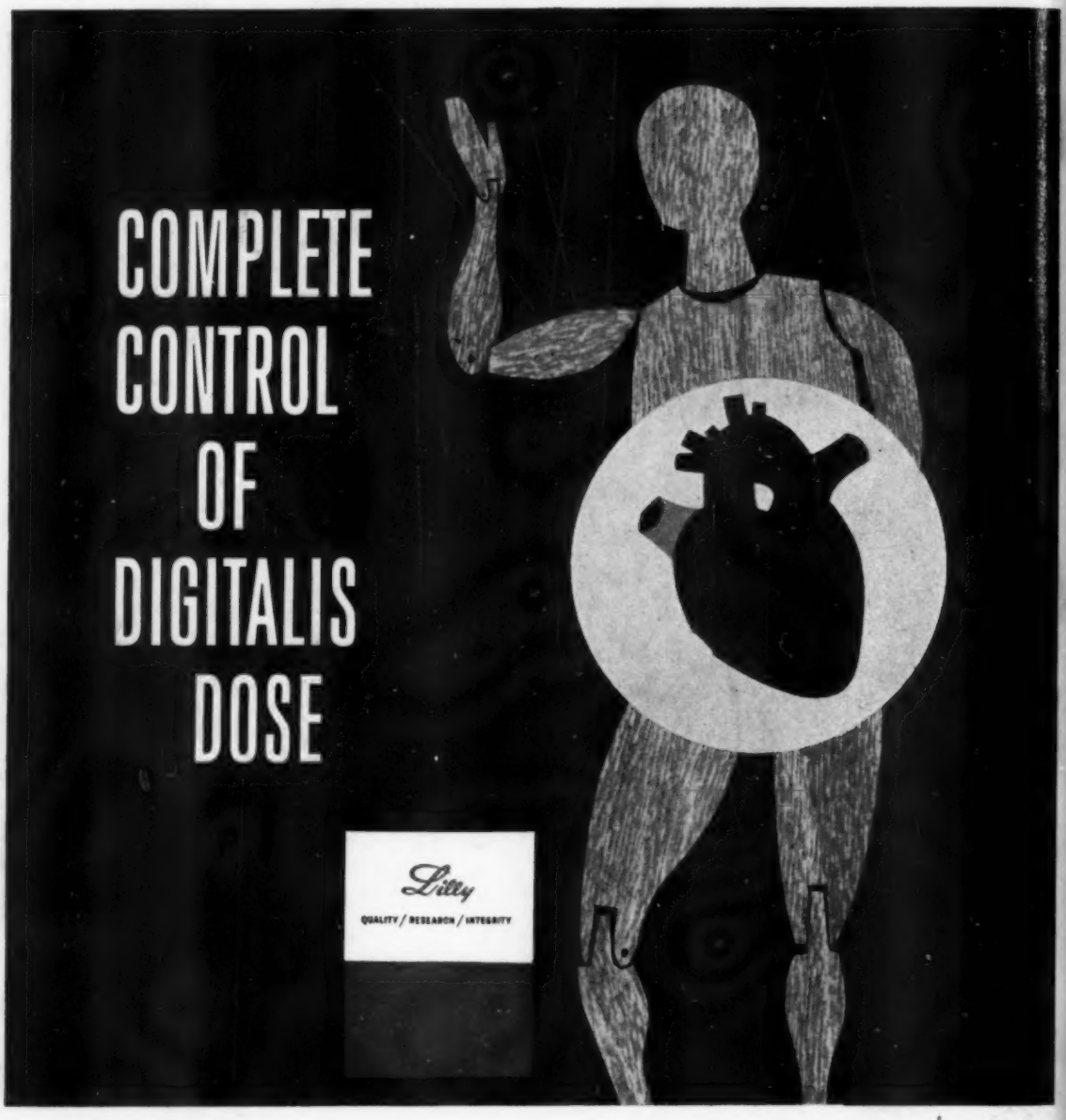

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